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# Clinical Medicine

## Original Articles for April, 1956

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*References:* **1. Pocock, D. G.: Personal communication. 2. Harding, C. W.: Personal communication. 3. Hollander, W. M.: Personal communication.**

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EDITORIAL

# Some Aspects of the Problem of Hypertensive Disease and Atherosclerosis*

*An evaluation of the progress in diagnosis, prognosis and the factors generally responsible for the development of these prevalent conditions*

JAMES M. NORTHINGTON, M.D., *Editor*

## DEVELOPMENT AND TREATMENT OF HYPERTENSIVE DISEASE

The many combinations of newer drugs for the treatment of hypertension are bewildering. Evaluation of current anti-hypertension regimens can only be approximate and may be considered as clinical impressions. It is too early to tell about the long-term effects on prognosis. We are going through the same stages in the revived medical treatment that we did in surgical treatment by sympathectomy.

The incidence of death up to five years of follow-up is three times greater in patients in groups II and III (moderate to severe hypertension) who have not had a sympathectomy or treatment with the newer drugs, than in a group of the same ages who have had a sympathectomy. The incidence of death (during a five year period) is 50% greater in the untreated patients in group IV (the most severe type of hypertension).

As to prognosis, the results from sympathectomy, and perhaps from the newer drugs, is better by 15 to 20% in women than in men. It is also better, in the same ratio, in untreated women than in untreated men.

Up to three years of results of

* As presented in a Symposium at the 64th Annual Meeting of the Association of Life Insurance Medical Directors of America, N. Y. C., 1955.

drug treatment in groups of patients with group IV hypertensive disease indicate that instead of the expected 85% of deaths if untreated, there were 45% of deaths in the treated group.

Does lowering the blood pressure in patients who already have severe hypertensive disease prevent or delay vascular complications, particularly coronary and cerebral arterial occlusion? At least one group of investigators (Rast and Orgain), in a follow-up of 61 patients treated for an average of ten months, found that it did not. Four of my 17 patients, who have had adequate and persistent lowering of blood pressure from hexamethonium for two years or longer, have had attacks of coronary occlusion—two of which were fatal attacks..

### TREATMENT OF CONGESTIVE HEART FAILURE

The sympathetic blocking drugs alone are effective in relieving congestive heart failure. These drugs may delay or prevent the concurrence of congestive heart failure in many patients with severe hypertensive disease.

Serious and unpleasant side effects still pose a problem, especially when large doses of the more potent agents are necessary to control the blood pressure. It should be kept in mind that, with the sympathetic blocking drugs, a good reduction in pressure occurs only when the patient is upright, that is during the daytime—and that, unless the patient sleeps standing up, his heart and arterial vascular system are subjected during one-third to one-half of the time to about the same stresses and strains as they would have without this treatment.[1]

1. Hines, E. A., Mayo Foundation, Rochester, Minn.

### CORONARY ARTERY DISEASE

Most physicians can achieve a correct diagnosis of angina pectoris, coronary thrombosis or coronary insufficiency in the great majority of cases by obtaining the proper history from the patient, and by the use of simple instruments including the ECG.

We know that in this disease, males predominate three to one, and that the disease afflicts more members of certain families and in the earlier decades than in other families. The well-set, muscular type is more vulnerable than the long and lean. Excess weight plays a role, although a more minor one. Likewise tobacco may be an aggravating factor, but only to a slight degree. As to the role the diet plays, we have no final answer. There is much to make us suspect that a diet high in fat may be detrimental. Regular physical exercise may possibly have a beneficial effect upon the development of coronary sclerosis.

That the number of coronary cases is constantly on the increase is a tribute to the medical profession's keeping people alive long enough to develop this condition, which has its maximum incidence in the seventh decade.[2]

### PRESENT CONCEPTS OF ARTERIOSCLEROSIS

It is now evident that while sex, individual peculiarities of metabolism and anatomy, blood pressure, daily physical exertion, and the use of tobacco influence the pace at which atherosclerosis develops and the sites at which it produces damage of clinical significance, the fundamental cause, subject to control, is the amount of cholesterol absorbed

2. Levine, S. A., Harvard Medical School, Boston.

from the gut. This depends, in turn, on the amount of cholesterol in the diet, and the amount of "blocking agents" contained in the diet. Vegetable foods, including vegetable fats such as corn oil and olive oil, contain blocking agents and lower blood cholesterol; animal products provide cholesterol, and animal fats contain minimal amounts of blocking agents.

Experiments of Ahrens, at the Rockefeller Institute, prove that fat, as such, and high-calorie diets do not raise blood cholesterol or the fraction which is associated with atherogenesis. Work at Harvard confirms the fact that low-protein diets aggravate, and hard physical work decreases, the effect of dietary cholesterol in raising blood cholesterol.

A rational management for those who have begun to suffer from, or are known to be predisposed to coronary disease, can be described. It is based essentially on a vegetarian diet, supplemented with lean meat and skimmed-milk products, and a life which keeps one in good physical training by such activity as walking, swimming and sports which do not impose violent exertion.[3]

3. Dock, W., State University of New York, College of Medicine, New York City.

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## Treatment of Manic Psychoses With Lithium?

Observations in 1949 by Cade that guinea pigs became lethargic on the injection of lithium promoted the staff of the mental hospital in Aarhus to give it to 48 patients in the manic stage of manic-depressive psychosis.

Tablets of lithium carbonate and lithium citrate, 0.3 gm. of the former salt per tablet, were issued together with placebo tablets in such a way that neither patients nor staff knew which was which. The patients' reactions were controlled in respect to hemoglobin concentration, sedimentation rate, leukocyte count, sugar and protein content of the urine, ECGS, and the lithium content of the spinal fluid.

There were eighteen patients whose improvement under this treatment was such that it could hardly be coincidental. In 21 others, the improvement might have coincided with such a spontaneous variation. The remaining nine patients did not respond. When the lithium was pushed beyond a certain tolerance, nausea and vomiting, diarrhea, general fatigue, slight drowsiness, and shakiness of the hands followed, but this passed when the lithium was withheld. The therapeutic value of this treatment is diminished by the risk of poisoning, which requires careful clinical and biochemical control. Because lithium does not act as quickly as electroshock, it cannot be expected to replace the latter treatment.

Foreign Letters (Denmark), *J.A.M.A.*, 4:327, 1955.

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ORIGINAL ARTICLES

# Breast Cancer During Pregnancy and Lactation

*Successful therapy can be effected without interruption of pregnancy by prompt treatment, usually by means of a radical mastectomy*

HARRY M. NELSON, M.D.,* *Detroit, Michigan* and
PEGGY JEAN HOWARD, M.D., *Louisville, Kentucky*

While it is true that cancer occurs most commonly in older persons, the disease is of vast importance at all ages and in both sexes. A recent large survey has shown that in newly-diagnosed cases of cancer, 30% of the men and 60% of the women had cancers in sites readily observable in regular physical examinations.

The problem of carcinoma of the breast during pregnancy or lactation arises often enough to concern every physician practicing obstetrics. Haagensen and Stout,[1] in 1943, stated that "cancer of the breast developing during pregnancy or lactation is so malignant that surgery cannot cure it often enough to justify this method of treatment." In 1951, however, they reversed their position and no longer considered the pregnancy itself in their criteria for operability.

In a period of 20 years, there has been a decrease of 16% in the annual mortality rate from cancer among women, this due largely to earlier diagnosis and better management of uterine cancer. We propose to show by illustrative cases that, in spite of the possible deleterious effects of pregnancy, cure can be effected in many of these cases, if diag-

*Associate Professor of Gynecology and Obstetrics Wayne University, Chief Gynecologist Woman's Hospital.

1. Haagensen, C. D., & Stout, A. P., *Ann. Surg.*, 118:859, 1943.

TABLE I

| Case | Age of Patient | Duration in Weeks Pregnancy | Symptoms | Extent of Lesion |
|---|---|---|---|---|
| 1 | 37 | 40 | 4 | Axillary metastasis |
| 2 | 37 | 28 | 20 | Distant metastasis |
| 3 | 35 | 16 | 2 | Local metastasis |
| 4 | 34 | 12 | 4 | Axillary metastasis |
| 5 | 21 | 12 | 4 | Inflammatory Ca. |
| 6 | 22 | 16 | 32 | Axillary metastasis |
| 7 | 29 | 18 | 0 | Distant metastasis |
| 8 | 39 | Lact. | 1 | Local metastasis |
| 9 | 34 | Lact. | 2 | Axillary metastasis |
| 10 | 34 | Lact. | 40 | Axillary metastasis |
| 11 | 27 | 18 | 5 | Local metastasis |
| 12 | 31 | 28 | 3 | Local metastasis |

In our series of 12 cases, the ages ranged from 21 to 39 years—average 31.6.

nosis is made early and adequate treatment is given promptly.

The incidence of cancer during pregnancy and lactation is stated to be 2 to 2.8% of all mammary cancers. In general, 3 obstetrical patients in 10,000 will have carcinoma of the breast. Results of various studies[2] indicate that 2% of all the women with mammary cancer had the disease during pregnancy and lactation. About 75% of the patients develop breast cancer during or after the menopause. Its highest prevalence is between ages 45 and 55, the highest birth rate between 20 and 25.

## EXTENT OF THE DISEASE

It has been shown[1] that the age of the patient is not related to the survival rate, but rather that chance of survival is dependent upon the extent of the lesion at the time treatment was instituted. In an analysis by Harrington of over 1,000 cases of carcinoma of the breast, the incidence of axillary metastasis in the non-pregnant group was 61%; in the pregnant, 95%. Sixty-six percent of our small series were found to have axillary or distant metastasis at the time of surgery. All but two of our patients having axillary or distant metastasis had been aware of a mass in the breast from one to 9 months before treatment was instituted. Engorgement and hypertrophy of the breast associated with pregnancy may mask the presence of a deep-seated, small or early tumor. In all our cases, the tumor was first noted by the patient. The patient should be taught breast self-examination. The obstetrician should examine the breasts at least twice during her pregnancy. Any mass in the breast found during prenancy or lactation should be biopsied.

## LOCALIZED MASS

*Illustrative cases.* A 35-year-old gravida IV, para III, in the 4th month of pregnancy, first noticed a lump in her left breast two weeks prior to her admission to Woman's Hospital in 1946. This was thought to be a fibroadenoma, but a breast biopsy revealed a grade-III medullary carcinoma. An immediate radical mastectomy was performed and no axillary metastasis was found. Recovery from operation was uneventful, and she was delivered of a normal, living infant at term. There has been no evidence of re-

2. White, T. T., *Ann. Surg.*, 139:9, 1954.

currence of the cancer to the present time (9 years later).

A second patient, aged 27, with a localized tumor, was operated on in 1940. She was in the 18th week of her third pregnancy at the time of the biopsy and radical mastectomy. There was no extension of the growth and she delivered spontaneously at term. There has been no recurrence. Five years after the radical mastectomy for reasons unknown to us, castration was performed by her family physician.

A 30-year-old primipara in her seventh month of pregnancy, noticed a small, painless lump beneath the left nipple. She called the attention of her physician to the mass. One week later biopsy showed adenocarcinoma, grade-III, and an immediate mastectomy was performed. No axillary nodes were found to be involved. Delivery at term was spontaneous. No further treatment is contemplated.

## DURATION OF THE DISEASE

Geschickter has shown[3] that of breast cancers first diagnosed during the first half of pregnancy, the average duration of symptoms was 6½ months. If the diagnosis was made during the latter half of pregnancy, the average was 8 months. Table I shows the duration of known symptoms and the duration of the pregnancy at the time the diagnosis was made in our cases.

## PROBABLE DELETERIOUS EFFECTS OF PREGNANCY

1. The early age of the patient
2. The increased vascularity of the breast
3. The intensity of endocrine influences, resulting in an increased rate of growth and spread.
4. The difficulty of detection of a mass in the presence of the increased fullness and size of the breast during pregnancy and lactation.

Since spread of a breast cancer is primarily lymphatic, we do not consider the increased vascularity during pregnancy of much importance. The tremendous supply of estrogen in the pregnant woman is deleterious to the breast cancer, but if diagnosed early and adequate radical mastectomy is done, the prognosis should be equal to that of cancer in the non-pregnant.

If the patient is well instructed in self-examination of the breast, the factor of delay in the detection of a mass can be lessened. Table II shows the extent of the disease, the treatment, and survival. Of the four patients having no metastasis, one is recent, one alive and well after 2 years, and the other two have no evidence of the disease after 6 and 9 years.

## TREATMENT

Except in obvious distant metastasis, primary treatment should consist of ignoring the pregnancy, regardless of its duration, and doing a radical mastectomy. If axillary metastasis is found after operation, a course of deep x-ray therapy should be given, without injury to the fetus.

If axillary metastasis has occurred, the prognosis is not always hopeless. A 37-year-old gravida V, para III, was admitted to the hospital, 39 weeks pregnant and in labor. A hard 4-cm. mass was palpable in one breast. The patient had first noted the tumor a month previously. At the time of delivery, a breast biopsy revealed carcinoma; 4 days later, a radical mastectomy was performed.

3. Geschickter, C. F., *Diseases of the Breast*, Ed. 2, p. 175, J. B. Lippencott, 1945.

TABLE II

| Extent of Lesion | Type of Treatment | Survival |
|---|---|---|
| 1 Axillary metastasis | Radical mastectomy & x-ray | L&W 22 years |
| 2 Distant metastasis | None | 2 weeks |
| 3 Local | Radical mastectomy | L&W 9 years |
| 4 Axillary metastasis | Radical mastectomy, x-ray therapy, abortion & castration | L&W 4½ years |
| 5 Inflammatory ca. | X-ray, testosterone & castration | 3½ months |
| 6 Axillary metastasis | Radical mastectomy & testosterone | 6 months |
| 7 Distant metastasis | Testosterone, castration, & adrenalectomy | 2 years |
| 8 Local | Radical mastectomy & x-ray | L&W 13 mos. |
| 9 Axillary metastasis | Radical mastectomy & x-ray | L&W 15 mos. |
| 10 Axillary metastasis | Radical mastectomy & x-ray & castration | L&W 3 mos. |
| 11 Local | Radical mastectomy | Recent |
| 12 Local | Radical mastectomy | 6 years |

Several large axillary nodes were found to contain carcinoma. She made an uneventful recovery and was given deep x-ray therapy to the left thorax, axillary, cervical and supraclavicular areas. Patient has remained well and has no evidence of recurrence in the 22 years since.

### THERAPEUTIC ABORTION

Only one patient was subjected to an abortion in our series. Except as a palliative procedure, and at the insistence of the patient and her husband, we do not recommend this treatment. If the cancer has not metastasized, nothing is to be gained by abortion. If metastasis has occurred, therapeutic abortion should only be considered as an adjunct to surgical castration, in hopes that the eradication of estrogen will slow down the spread of the disease.[4,5]

*Illustrative Case:* A 34-year-old gravida III, para II, 4 months pregnant when admitted with a 7-cm. mass in the left breast, and a 2-cm. mass in the left axilla. The patient had been aware of the tumor for a month. Following frozen section diagnosis of cancer, a radical mastectomy was performed. Many axillary metastases were found Three weeks later, a subtotal hysterectomy and bilateral salpingo-oophorectomy were done, at the request of the patient and her husband with the understanding that it was only a palliative procedure. X-ray therapy was then given—a total of 8,600*r*—to the left supraclavicular, axillary and left anterior and posterior oblique chest wall areas. There has been no evidence of recurrence in the 4½ years since.

### INFLAMMATORY CARCINOMA

Of the 12 breast cancers in our series, only one was inflammatory—the usual ratio. This condition is not always easy to diagnose. Da Costa[5] has stated: "In any case of supposed mastitis persisting for more than two weeks, biopsy is indicated to rule out inflammatory carcinoma."

*Illustrative case:* Our patient was a 21-year-old gravida, para O, admitted 4½ months pregnant. One month prior to admission, a diffuse, reddened, tender swelling of the

4. Harrington, S. W., *Ann. Surg.*, 106:690, 1937.
5. Da Costa, J. C., *Modern Surgery*, Ed. 8, p. 1585. Philadelphia, W. B. Saunders Co., 1919.

left breast had been treated with sulfa and penicillin, without improvement. The right breast soon became involved. In the hospital, diagnosis of bilateral inflammatory carcinoma was confirmed by biopsy. A total dosage of 6,160r was given to both breasts and testosterone propionate, 100 mg. daily, was started. The breasts rapidly regressed in size and the symptoms improved. She was discharged from the hospital and continued satisfactorily on testosterone for two months. When last admitted, in the 28th week of gestation, she showed evidence of generalized metastasis, had a blood dyscrasia, and in spite of daily blood transfusions, it was impossible to raise her hemoglobin above 8 gms. At 30 weeks, she was delivered by Caesarian section of a normal, living infant, and both ovaries removed and found to contain extensive metastases. In spite of the castration and continued testosterone therapy, she failed rapidly and expired 5 days later. Had therapeutic abortion been done, the patient's life would probably not have been prolonged by more than a few weeks.

### ENDOCRINE THERAPY

The endocrines, particularly androgens, have been widely used in recent years, and proved to be valuable adjuncts in the palliative treatment of breast cancer. Their greatest usefulness is in treatment of bone metastasis. They should be reserved for palliation and when x-ray will no longer control the pain of bone metastasis.

Androgens are occasionally useful in soft tissue metastases. Both dosage and drug must be individualized to fit the needs of the patient. The minimal amount of androgen, which will control the patient's symptoms should be used. The production of acne, coarse voice, and hirsutism must frequently be overlooked in deciding the dosage of the androgen.

To eradicate estrogen if the patient is premenopausal, surgical castration should be considered. This procedure should be reserved as a therapeutic agent, particularly in the treatment of bone metastasis.

### CORTISONE TREATMENT

If, after surgical castration and androgen therapy, further treatment is indicated, some palliation may be obtained by the use of cortisone. The work of Huggins on bilateral adrenalectomy is familiar to all of us. The following case is representative of what can be expected in a well-selected estrogen sensitive case.

*Illustrative case:* A 29-year-old gravida II, para I, 4½ months pregnant was admitted because of malaise, weight loss and severe, constant backache. X-rays showed osteolytic lesions of the spine, pelvis, ribs, skull and humerus. After repeated careful examinations, a small tumor was found in the right breast, which, on biopsy, proved to be carcinoma. On the next day, spontaneous abortion occurred.

Because of the extent of the metastasis, x-ray therapy was thought inadvisable, so testosterone propionate was begun, with a minimum of palliation. She was then placed on adrenal cortical substitution therapy, and bilateral oophorectomy and adrenalectomy were done in three stages because of the extreme debility of the patient. Nine days following the third operation, the patient was able to sit up for the first time in 3 months. She continued to improve and was discharged, walking, 3

weeks later. She remained ambulatory and comfortable for 2 years. Death was from pulmonary metastasis.

### PROGNOSIS

Harrington[4] has found that carcinoma of the breast without axillary metastasis in the non-pregnant patient carries a 5-year survival rate of 72.1%. In those pregnant but without axillary metastasis, the 5-year survival was 61.5%. If axillary mestastasis was present, the 5-year survival decreased from 28% to 5.7% in the pregnant or lactating group. Again we emphasize that an early diagnosis is possible if the physician and the patient are constantly aware of this condition.

### SUBSEQUENT PREGNANCIES

We would agree with Cheek[6] that, in the absence of axillary metastasis, and no recurrences of the cancer in 3 to 5 years, another pregnancy may be undertaken. Haagensen[1] thinks that, as follow-up care improves, the incidence of bilateral breast carcinoma will approach 10%. This does not imply that pregnancy has any influence on the development of breast carcinoma, but that an already existing cancer will have an accelerated growth during pregnancy and lactation.

6. Cheek, J. H., *Arch. Surg.*, 66:664, 1953.

### SUMMARY

Twelve cases of carcinoma of the breast occurring during pregnancy and lactation have been presented, the average patient age 31.6 years. In 8 of our 12 cases, axillary or distant metastasis had occurred at the time they were first seen. The average duration of symptoms in those having axillary or distant metastasis was 13.2 weeks.

It can be concluded that:

1. There is still delay in undertaking treatment for this disease on the part of both patient and physician.
2. Pregnancy alone does not make this cancer incurable.
3. Any lump in the breast found during pregnancy or lactation, should be biopsied.
4. There is rarely cause for interrupting a pregnancy in treating cancer of the breast.
5. Unless distant metastasis is found from a bone survey before surgery, a radical mastectomy should be done.
6. X-ray, androgens, castration, and occasionally adrenalectomy in the far-advanced cases can do much in palliation of a metastatic breast carcinoma.

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## The Cross-eyed Child

The wearing of spectacles, even in an infant, is of great importance if there is a significant refractive error. It represents sufficient treatment in ⅓ of the cases of convergent strabismus. If the wearing of glasses is delayed, it may become difficult to obtain a good functional result.

Authorities are agreed on the point that early treatment of the cross-eyed child is essential.

The family doctor should be on the lookout for those conditions and should encourage the parents of such children to seek advice as soon as the condition is discovered.

Braley, A. E., et al., *J. Iowa M. Soc.*, 45:185-187, 1955.

# New Radiopaque Medium for Excretion Urography—Hypaque: A Preliminary Report of 300 Cases

*An improved diagnostic procedure with an increased margin of safety that permits a fine delineation of many of the minor calyces*

H. B. HERMANN M.D. and N. R. HERMANN, M.D.,
*Brooklyn, New York*

Since the first report by Swick in 1929[1] of an iodine-containing organic compound for excretion urography, urologists have continued the search for a better radiopaque medium with a high degree of radiopacity, a low toxicity and a rapid rate of excretion.

The several urographic media which have been used with some measure of success in excretion urography are iodopycracet (Diodrast)[2], sodium iodomethamate (Neo-Iopax)[3] aid sodium acetrizoate (Urokon)[4]. All of them have had a certain percentage of undesirable reactions.

Hypaque sodium* has been used for excretion urography in 300 consecutive unselected cases by the authors. The increased contrast with a minimal percentage of minor side reactions indicate that this new radiopaque medium, with its greater safety, more nearly approaches the ideal excretory urographic media than any of those currently avail-

1. Swick, M., *Klin. Wchnschr.*, 8:2087, 1929.
2. Moore, Thomas D., *J. Urol.*, 30:127, 1933.
3. Sugar, Herbert, *West J. Surg.*, 40:320, 1932.

*Hypaque (brand of diatrizoate) sodium, supplied by Department of Medical Research, Winthrop Laboratories, Inc., New York 18, N. Y.
4. Nesbit, Reed M., Nesbitt, Tom E., *Univ. Hosp. Bull., Ann Arbor*, 18:225,1952.

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able. Our experience with Hypaque in these respects closely approximates that of Moore and others.[5,6,7,8,9]

## PREPARATION

The usual preparatory routine of a laxative of magnesium sulfate and dehydration was followed in most instances in the same manner as with other excretory urographic media. One patient presented himself without prior preparation with an indication for an intravenous pyelogram, and it was decided to go on with the procedure. The results with Hypaque gave a diagnostic film with excellent concentration of Hypaque in the upper urinary tract. This suggested that perhaps routine preparation may not be necessary with Hypaque. Several other patients have been examined without preparation; all have had satisfactory diagnostic films. Until a larger series has been done we will not know whether or not to omit the usual laxative and dehydration preparation. Slight compression with a table band was routinely used in most cases.

## PRECAUTIONARY MEASURES

Serious reactions, including fatalities attributed to allergic hypersensitivity, have occurred with excretory urographic media. They are rare, however, in ratio to the millions of cases in which they have been employed.

Precautions which have been recommended[6] include:

1. Taking the history of personal and familial allergies (e.g. bronchial asthma, hay fever, eczema), of previous iodine studies, and of sensitivity to iodine and other drugs.
2. Making a preliminary sensitivity test.
3. Giving preliminary antihistaminic medication.
4. Injecting the contrast medium slowly.
5. Having medications available for emergency use.

Many physicians make a preliminary test for allergy to urographic media. A careful clinical history, with particular emphasis upon allergy, and studied clinical judgment still remain essential in this field of medical practice. Although the evidence favoring the use of antihistaminics seems encouraging, no definite conclusions can yet be drawn. Some favor the oral use of an antihistaminic at bedtime the evening before the examination, and a second dose one hour before the urogram is started.

## SENSITIVITY TEST

Methods to detect sensitivity to urographic media include ocular, oral, intradermal and intravenous testing. The ocular, oral and intradermal tests are not reliable since reactions to them are more often due to a direct local vascular effect.[10]

An intravenous test is more likely to show sensitivity, although a negative test does not necessarily rule this out. A small dose (0.5—1 cc.) is slowly injected intravenously (taking one minute) followed by observation for twenty minutes to detect delayed reactors. Warning signs and symptoms of possible intolerance or allergy are:

1. Respiratory difficulty:
   a. Dyspnea or sensation of suffocation

5. Moore, T. D., Mayer, R. F., *South. M. J.*, 48:135-141, 1955.
6. Council on Pharmacy and Chemistry, Diatrizoate sodium, *J.A.M.A.*, 159:681, 1955.
7. Lowman, R. M. et al., *Surg. Gynec. & Obst.*, 101:1, 1955.
8. Rollins, et al., *Am. J. Roentgenol.*, 73:771, 1955.
9. Root, J. C. & Strittmatter, W. C., *Am. J. Roentgenol.*, 73:768, 1955.
10. *N.N.R.*, 1954, p. 336.

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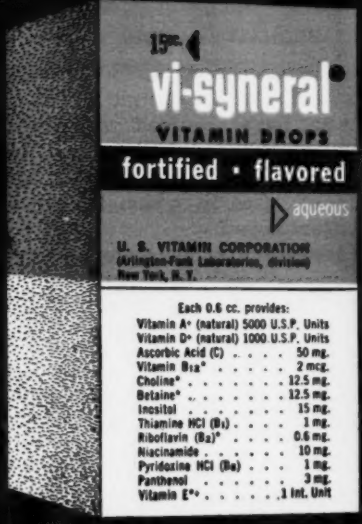


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TABLE I

Quality of Excretory Urograms with Hypaque

| | |
|---|---|
| Satisfactory for diagnosis | |
| Excellent | 225 ( 75%) |
| Good | 66 ( 22%) |
| Not satisfactory for diagnosis | |
| Poor | 9 ( 3%) |
| Total | 300 (100%) |

b. Tightness in throat.
2. Sneezing, itching or urticaria.
3. Nausea or vomiting.
4. Fainting.

If no reaction occurs to the test dose, the remainder of the dose is injected slowly while observing the patient continuously. Should any evidence of a sensitivity reaction appear, the injection is stopped and, if necessary, treatment given.

### EMERGENCY TREATMENT OF REACTIONS

Suggested drugs are Benadryl Hydrochloride, 10 mg. or 1 cc., intravenously for the patient who exhibits severe nausea, marked urticaria or slight respiratory embarrassment. If the reaction is severe with marked respiratory embarrassment and signs of impending shock, 50 mg. of a cortisone preparation is given intramuscularly.

Patients with a personal history of allergy (particularly bronchial asthma), especially if accompanied by a familial history of allergy, who also have a positive sensitivity test should not be given the urographic agent intravenously. If the test is positive in the absence of a history of allergy, many physicians consider the injection of the full dose inadvisable, while others believe it may be given very cautiously if there is an urgent need for the examination.

### TECHNIQUE

Since the authors have found no useful correlation between an intradermal sensitivity test and possible reactions only the intravenous test was used. Routinely 1 cc. of Hypaque was injected intravenously and in this series of 300 cases there were no reactions to the 1 cc. test dose. After four or five minutes the full dose of 30 cc. of Hypaque in adults was injected slowly. Depending upon the age children were given 10 to 15 cc. of Hypaque, ⅓ to ½ the adult dose.

Films were taken routinely at 5 and 15 minutes, the 5 minute film giving the best contrast in most cases. When indicated, a 25 minute film or later was taken.

Since Hypaque gives a satisfactory contrast and delineation of the upper urinary tract, the number of retrograde urograms have been reduced to a minimum. For retrograde urography 5 to 15 cc. of a 1 to 1 dilution of Hypaque and sterile water has given excellent results.

### CHEMISTRY AND PHARMACOLOGY

Hypaque sodium is sodium 3, 5-

TABLE 2

Side Effects with Hypaque

| | | | |
|---|---|---|---|
| 1. None | | 258 | ( 86%) |
| 2 Present | | 42 | ( 14%) |
| a. Severe | None | | |
| b. Mild | | | |
| Nausea | 40 | | |
| Generalized urticaria and burning sensation | 1 | | |
| Urticaria of lip | 1 | | |
| Total | | 300 | (100%) |

diacetamido-2,4,6,-triiodo benzoate ($C_{11}H_8I_3N_2NaO_4$) with a molecular weight of 636.0 which contains 59.87% iodine and is highly water-soluble. It comes in a 30 cc. ampul in a 50% solution.

Pharmacodynamic studies[11] of acute intravenous toxicity studies in mice, rats and cats show the $LD_{50}$ of Hypaque sodium to be about from 10,000—12,000 mg./Kg. This is 50 times the normal diagnostic of 30 cc. of Hypaque. At the dosage level of 2,000 mg./Kg. daily in monkeys (ten times the diagnostic dose), body weight, general appearance, hematologic findings (including red and white blood cell counts, differential counts and hemoglobin concentration) and postmortem examinations of the kidneys, liver, lungs and spleen were all normal. In the dog, no significant changes in heart rate, blood pressure, respiration of effects upon autonomic functions were observed in doses of 500, 1000, 2000 and 4000 mg./Kg. administered intravenously successively. These data amply demonstrate the relative lack of toxicity of Hypaque.

The 291 (97%) patients out of 300 with films satisfactory for diagnostic purposes include 225 (75%) excellent films showing fine delineation of the upper urinary tract and 66 (22%) with good delineation of the upper urinary tract. This significantly high percentage of satisfactory films represents a distinct advance in excretory urographic diagnostic procedures. The sharpness of the minor calyces in many of the films has been of particular interest since these are rarely so well delineated with other media.

## SIDE EFFECTS

In this series of 300 cases with Hypaque there were no reactions to the intravenous *test* dose, and no major side effects observed during or after the *diagnostic* dose. There was a history of asthma and a single or multiple allergy in 60 (20%) patients, all of whom were given Chlortrimeton one hour before their intravenous injection. There were no severe or frank vomitings in the entire series. Although a small quantity of Hypaque was inadvertently injected outside the vein in six pa-

11. Data in the files of the Department of Medical Research, Winthrop Laboratories, Inc., New York, New York.

tients, there was no vein or arm pain in these or in any other patients in the series.

The full 30 cc. dose was given to 260 patients. Of the two developing urticaria, one was generalized, the other on the lip, both appeared 15 minutes after the injection, and both disappeared one hour later. If a patient developed nausea during the injection it was stopped or slowed up immediately. When this happened most of these patients were given only ½ the full dose—15 cc. of Hypaque; in all these there was adequate visualization for diagnostic purposes.


SUMMARY

A series of 300 consecutive cases are reported using a new radiopaque medium, Hypaque sodium, for excretion urography. There was good or excellent concentration of Hypaque in the upper urinary tract in 97% of this series. Of particular note is the fine delineation of the minor calyces in many instances. These calyces are rarely seen when other media are used. The increased contrast with a minimal percentage of minor side reactions indicates that this new medium has an increased margin of safety and more nearly approaches the ideal excretory urographic medium than any of those currently available.


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## Eosinophil Cell Count Pre- and Post-Operative

Preoperative eosinophil cell counts in 31 and postoperative counts in 79 patients were made. Preoperative eosinopenia (in average 33 cells/cu.mm.) was established in 16 cases in which the blood samples were taken 1 to 4 hours prior to the operation. Eosinopenia was observed after minor operations in 29 out of 37 cases and after intermediate and major operations in 39 out of 40 cases. The rise in eosinophil cell count to the normal level seems to differ in type after major and minor operations: after major operations eosinophilia (more than 200 cells/c.mm) was found in 11 out of 23 cases, whereas only one case of eosinophilia followed the minor operations on the fourth day after operation. Three of the cases studied terminated in death. In all these cases eosinopenia of longer than normal duration was observed. In one case where the cause of death was a development of peripheral and pulmonary edema, a prolonged excessive secretion of mineralocorticoid hormones might have had a deleterious effect and should have been studied.

Antila, L. E., *Ann. Chirurg. et Gyn. Fenniae*, 43, Sup. 5:9-20, 1954.

# Clinical Aspects of Automobile Accidents and Injuries

*A long-range program should be established by physicians through their county medical societies for improved driver licensure standards*

JACOB KULOWSKI, M.D.,* *St. Joseph, Missouri*

There are three well defined approaches to the problem as a whole; i.e., prevention, reduction of injuries and aids to recovery. This means physical fitness and its maintenance in regard to drivers, valid medical data on crash injuries and deaths; first aid, emergency care, definitive diagnosis and treatment; and rehabilitation (medical and medico-legal).

## MEDICAL STANDARDS OF DRIVER LICENSURE

Motorist safety is dependent upon driver proficiency, highway facility and automotive safety engineering. Driver proficiency is interlocked with driver education and training, and law enforcement. The last may very well prove to be the core of a program of traffic safety, and it needs assistance from every possible source. Important in this regard could be the establishment of adequate medical standards of driver licensure. A careful physical examination at the time the prospective driver (or renewal applicant) contacts the traffic authority would have great implications.

On the basis of the physical examination alone, three possibilities are apparent in regard to driver li-

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censure; i.e., refusal of permit, full permission to operate an automobile; and a restricted type of permit. The last could restrict driving speeds; day or night or bad weather driving; and, above all, forbid carrying passengers. A learner's permit would be granted first to those meeting requirements at the time of application for a driver's license.

The physical disqualification of major importance is inadequate vission. Other disqualifying or restrictive physical states should include epilepsy, diabetes, malignant hypertension, advanced cardiovascular-renal disease, and gross physical defects. Also important are certain psychologic, psychiatric and psychosomatic states. Addiction to narcotics and alcohol deserve special emphasis. Also the use of medication such as the tranquilizing drugs, or drugs which tend to lengthen the time a person can stay awake. Those who are recovering from illnesses and operations may not be fit to drive. The wearing of cumbersome appliances ought to be carefully assessed.

## REDUCTION OF INJURIES

This involves crash-impact safety engineering features. Valid medical data are essential to engineers and designers. Clinicians must differentiate between morbidity among survivors and post mortem findings. This distinction should stimulate further investigations along pathologic lines in the latter category; the paucity of such data is disturbing to all students of this problem.

## PATHOLOGIC ANATOMY

The variable results of automobile crashes and/or upsets is best reflected in the clinical effects; those who escape injury; those who are injured and survive; those who are killed immediately; and those who survive the immediate effects of their injuries but die at a later date. Among survivors a definite pattern of injury has emerged from statistical studies made thus far. Criteria of crash effects are best studied from the standpoint of topical lesions, fractures and internal injuries. The general order of frequency of injury to the different body areas appears to be in this order: extremity, head, face, chest, trunk and pelvis, neck and abdomen. Internal injuries occasionally result without concurrent overlying fractures; e.g., head and chest injuries in some 25 per cent of cases.

Internal injuries vary greatly in the different body cavities of survivors, but consist chiefly of cerebral concussion and more gross lesions in the head, chest and abdomen.

About 80% of crash survivors suffer more than two injuries. There are instances of immediate death from primary shock in head and chest injuries.

## PATHOLOGY

About 15 percent of motorist deaths occur at the scene of accident; the remainder after varying periods of time in the admitting or other room of a hospital or after discharge. The vast majority of the deaths occur within 48 hours after hospitalization. Causes of deaths in these two major subgroups—early and later—are best considered on the basis of primary and secondary shock. The first includes a tremendous cardio-respiratory jolt with circulatory failure; the second type implies the same, plus contributory factors or complications.

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motorist injuries are injuries to organs above the diaphragm. In the 29 cases studied by the writer, one third showed evidences of injury to the mediastinal structures—chiefly the heart and the great vessels. Most of the latter contributed to death.

### AIDS TO RECOVERY AFTER INJURY

There are three subgroups of fatality: immediate, intermediate (within 48 hours) and delayed deaths. Motorists found inside cars after accidents are either dead or seriously injured. Reduction of immediate deaths is largely a matter of improved crash-impact engineering.

First aid is a primary and urgent consideration. Rapid (but safe) transport to a hospital is of major importance. An open airway precludes all other measures; and is best achieved with the victim lying on the side during transport. Wounds should be dressed and fractures splinted, however primitively. First-aid measures need revision as to simplicity and applicability. Here is a job for all doctors to put their minds to, instead of leaving it to the manufacturers and splint designers.

Hospital emergency facilities need to be expanded to meet the need for restitution of blood volume, cardiac resuscitation, pulmonary ventilation and other procedures which, used immediately, would go far toward relieving the burden of in-patient care.

Diagnosis and treatment of the more serious cases calls for changes in policies rather than changes in techniques. A more vigorous policy of diagnosis is needed. Internists and all other types of specialists should have a more active part in the care of these people. The majority of internal injuries could be handled conservatively — medically rather than by surgery. Those with intra-cranial and abdominal injuries need neurosurgical and general surgical participations, respectively. Need for orthopedic aid is obvious, but frequently overlooked.

### RESIDUAL DISABILITIES

The majority of the disabling conditions are more or less orthopedic in nature. The medico-legal aspect is important. The commonest disabilities include "whip-lash" injuries of the neck and low back—the former often concurrent with pre-existent osteoarthritis, the latter with congenital and other conditions of the low back. The responsibility of motor accidents for herniated or ruptured disc, especially in the cervical region, is hard to establish. Given similar opportunities for study, the diagnostic error is no greater in litigated than it is in non-litigated cases.

### GENERAL COMMENTS

The basic responsibility of doctors lies in the diagnosis and treatment of any and all kinds of these injuries. The establishment of adequate medical standards of driver licensure programs must be accomplished through the county medical society. These societies must initiate and carry through such a program. Visual defects must be evaluated; then other major physical and psychologic states which lessen driver proficiency. A beginning must be made in every county medical society. This is a basic challenge to the carrying out of a long-range program.

### CONCLUSIONS

The clinical aspects of automobile accidents and injuries are clear-cut and should be the least controversial of all the phases of our ever-increas-

g traffic problem.

The doctor's responsibilities in this spect are intertwined with individual and community needs along ese lines.

His first duty is to organize the unty medical society for better medical standards of driver licensure.

Next, doctors, as individuals and as groups ought to join with citizen's committees in focusing attention upon automobile accident prevention first, last and always.

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## efractory Congestive Heart ailure in the Elderly Patient

It is difficult to recognize the early gns of decompensation in the elderly patient. Left ventricular failure ould be suspected from cough, hortness of breath or exertion, orthopnea, and particularly paroxysmal nocturnal dyspnea. Persistent ales at the lung bases may mean ulmonary congestion or edema, instead of bronchitis. There are often e additional findings of pulsus alernans or a gallop rhythm. Right entricular failure usually appears fter the left ventricle fails in diffuse coronary atheromatosis or hypertension. Congestive heart failure produces distention of the neck veins, dependent edema and a tender, enlarged liver.

The physician must re-survey critically the symptoms and signs and ascertain that they are due to congestive heart failure rather than other causes.

When a patient with congestive heart failure fails to respond to the usual measures, one must make certain that the predisposing conditions have been adequately dealt with, that the precipitating causes have been controlled, and that perpetuating factors have not been overlooked.

The most common precipitating factor is infection. This increases metabolism, interferes with oxygenation if in the lungs, and it has a toxic myocardial effect. The second cause is undue physical activity, even the effort of labored breathing or pulling on of a girdle. If necessary, use sedatives and narcotics temporarily. Repeated pulmonary embolism, unsuspected, may be the reason why there is continuing dyspnea and edema.

Refractory congestive heart failure is managed similarly in all age groups; in the elderly, coronary atheromatosis is a more frequent etiologic factor.

Proper therapy of precipitating, contributing, and perpetuating causes is essential.

A review of the therapy may bring about changes with gratifying results. Proper attention must be paid to the restriction of sodium, limitation of activity, adequate digitalization and the optimum use of diuretics.

The geriatric patient is especially susceptible to electrolyte complications and less able to withstand electrolyte imbalances and maintain reparations by solutions. Correction of serum and electrolyte balance may again make the failure responsive.

Hejtmancik, M. R., et al., *Texas State J. Med.*, 5:238-243, 1955.

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# A Clinical Evaluation of Nicozol as a Cerebral Stimulant for the Aged

*Many problems associated with the care of elderly patients with mild psychiatric symptoms may be mitigated by use of this preparation*

LLOYD J. THOMPSON, M.D.,* and
RICHARD C. PROCTOR, M.D.,** *Winston-Salem, North Carolina*

Much research is now being directed toward finding drugs and methods for alleviating the disturbing symptoms associated with the aging process. One goal of this therapy is to make it easier for families to take care of patients at home. Generally, the earlier patients are treated the better the results. Since many aged persons show only the more common evidences of simple early brain deterioration, it would be ideal if they could safely remain in their community and be adequately treated in the home. Such treatment must be simple, economical, practical and safe to be accepted by both physicians and families of patients.

At the present time, more than one-third of all persons first admitted to public mental hospitals in the United States are over 65 years of age, and by 1980, 26 million of us will be 65 or older. Casual recognition of this fact will indicate that the problem of emotional disorders of the aging will become increasingly more prevalent. The burden that will be placed on our institutions is obvious, unless more patients can be successfully treated at home.

Our recent study[1] of 60 aged hospitalized patients with psychiatric

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1. Thompson, L. J., Proctor, R. C., *North Carolina M. J.*, 15:596, 1954.

symptoms—from mild confusion and memory loss to the picture of aggressiveness, hostility, disorientation and marked confusion—indicated to us that many of these patients could be safely, economically and adequately treated in their own homes. We were able to obtain improvement in 46 of these 60 patients. They were given one teaspoonful of Nicozol* 30 minutes before each meal. This is a preparation containing Pentylenetetrazol (200 mg./tsp.) and nicotinic acid (100 mg./tsp.) in a lactate of pepsin base containing only 5% alcohol. Pentylenetetrazol, a synthetic organic tetrazol derivative, has long been employed as an effective respiratory and circulatory stimulant. It exerts an intense stimulating action on the central nervous system, acting primarily on the higher centers of the brain. While it acts mainly on the respiratory, vasomotor and vagal centers of the medulla, all parts of the cerebrospinal axis are stimulated to some degree. It is a potent analeptic agent whose action is most evident when the higher brain centers are depressed, as in illness of old age, barbiturism, or alcoholism. Thus one might well expect Pentylenetetrazol to improve pulmonary ventilation and circulation and help overcome the anoxia frequently present in the aged, depressed or fatigued.

## ADVANTAGES OF NICOTINIC ACID

Nicotinic acid is a potent vasodilator and has been successfully employed by others[2] in treating the confusional states and psychoses of senility. Whether its beneficial effect is due to cerebrovasodilation or a direct physiological action on brain cell function is not clear. Regardless of its mode of action, a formulation containing both Pentylenetetrazol and nicotinic acid has produced very gratifying results. It has no unfavorable effect on blood pressure or hypertension, though it actually will lower both systolic and diastolic readings in hypertensives to a mild degree. It has had no adverse effect on body temperature, pulse rate, respiratory rate, or blood chemistry. Usually its use will promote appetite, and sleeping habits will be improved.

## CASE HISTORIES

In order to demonstrate how successfully the general practitioner can treat these patients in their homes, two cases have been selected for presentation, one of which previously required hospital care.

*Case 1.*—A 68-year-old widow entered the hospital on March 24, 1954, because of emotional difficulties dating back two years, when she first noted feelings of depression and general restlessness. Six months before admission, she became more worried, began to lose weight and lost interest in her usual activities. She became more restless, had difficulty with concentration and required hospitalization.

On admission she showed evidence of recent weight loss and of generalized arteriosclerosis, and there were sclerotic changes in the fundi. Blood pressure was 124/70, heart size and contour normal. Neurological examination showed only some slowness in reaction time and slight unsteadiness of fine movements. Laboratory data: urine negative, RBC normal, HqG. 12.5 gr., WBC

*The Nicozol used in this study supplied by Drug Specialties, Inc., Winston-Salem, N. C.

2. Levy, S., *J. A. M. A.*, 153:1260, 1953.

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6,700—with a normal differential. Fasting blood sugar was 109 mg. and serologic tests negative.

Mental status: a tense woman showing signs of general agitation and difficulty in concentration. She was very discouraged and concerned over her difficulty in sleeping and her memory difficulty. She scored 86 on the Wechsler-Bellevue Intelligence Test, and the performance suggested generalized impairment or deterioration of intellectual processes. Her general information, judgment and abstraction were extremely limited. The Bender-Gestalt drawings revealed signs of gross impairment. The Rorschach test revealed perplexity, impotence and confabulatory thinking—all of which seemed to be related to organic brain disease.

She was placed on Nicozol—one drachm 30 minutes before each meal —and given light doses of insulin to stimulate her appetite. Over the next few days she gradually improved in both behavior and thinking processes and was discharged on April 9, 1954, as improved. Since that time she has remained at home and maintained her improvement. She has continued on the medication to the present time.

*Case 2.*—A married white farmer, 62 years of age, was seen in the office on January 3, 1956. His son brought him in for evaluation. The patient was unable to remember his age, but when reminded of it, recognized it. The son said the patient had a marked memory loss, rambled around the house and farm and at times got lost. He had lost his appetite and slept poorly. He believed he had been married 10 years (though he has three children over the age of 20). He was agitated, restless and confused; blood pressure was 190/90. There was an aortic systolic murmur (Grade 2), which was not transmitted. Fundi showed tortuosity and narrowing of the arteries.

The patient was placed on Nicozol capsules (each containing ½ the strength of 1 tsp. of the elixir) 1 capsule before each meal and at bedtime. Seen again on January 31, 1956, in the office, the son said his father was less agitated, was eating and sleeping well, and did not wander away anymore. The patient himself appeared more relaxed and was not restless; he showed less evidence of confusion, though his memory was still impaired.

## SUMMARY


1. Two cases are presented of patients with behavior disturbances due to organic brain damage associated with the aging process.

2. Treatment with Nicozol is described.

3. In our opinion Nicozol is a practical, safe, effective and easily controlled preparation for the treatment of the aged mental patient. It is particularly helpful for those with only mild memory defects and confusion, and is less helpful in patients who have had prolonged illness and in whom organic brain deterioration is marked.

4. Nicozol should be prescribed as soon as evidence of senile retrogression is observed, in an effort to delay as long as possible the necessity for hospital care and treatment.

# Gastro-Intestinal Hemorrhage: Practical Considerations in Diagnosis and Treatment*

*Indications that will help to prevent uncertainty regarding the diagnosis and aid in the selection of emergency measures*

SAMUEL MORRISON, M.D.,** *Baltimore, Maryland*

Massive upper gastrointestinal hemorrhage, sometimes referred to as critical hemorrhage, is characterized by severe hematemesis and melena, one or the other or both together. Although there have been many such cases, it appears that each time a massive upper gastrointestinal hemorrhage appears in the hospital, the reaction is one of uncertainty. We have a standard operating procedure, but there is doubt concerning the diagnosis and the application of emergency treatment.

Patients seen recently include a young boy of 12 who bled profusely and subsequently was found to have a duodenal ulcer. The general impression was that such hemorrhage in youngsters is uncommon; but, according to Ivy, it is not infrequent. The real difficulty is that these patients do not receive X-ray examinations, and therefore a definitive diagnosis is not made.

Another patient, a woman, came in for her second hemorrhage, which was as severe as the first one. The surgeon who was consulted hesitated about operating. The X-ray was negative, and the gastroscope revealed a gastritis. Because she

*Abstract of Lecture delivered by invitation on November 30, 1955, at the Veterans Administration, Baltimore Regional Office, Medical Division.

**Associate Professor of Medicine and Associate Professor of Gastro-Enterology, University of Maryland School of Medicine.

wished it, and because the doctor in charge thought it advisable, the surgeon opened her stomach, but could find no bleeding area. However, a resection was done. Two hours after the operation, we looked at her stomach fixed in formalin and there, unmistakably, was an ulcer the size of a penny. It is difficult to understand how such an ulcer could be missed by the various modes of examination. This case would have been listed as one of massive hemorrhage, cause undetermined, except for her operation.

Then there was the service patient who had received many transfusions before the surgeons were consulted. They would operate when the condition was safe, but the patient never reached that point. After 27 transfusions which more than doubly replaced his circulating blood, he died; at post-mortem, a competent pathologist was unable to find the source of bleeding. These cases are cited to show how difficult can be the quest for diagnosis in some of these bleeding patients.

## MULTIPLE TRANSFUSIONS

When a patient appears in the hospital with a severe hemorrhage, the question always arises whether emergency diagnosis or emergency treatment is more important. In my judgment, emergency treatment is the more important, and this treatment comes down to the administration of blood. Prior to 1930, very few transfusions were given to bleeding patients because it was felt that they would stop bleeding as the blood pressure fell and as the coagulation factors came into play. Then came the era when transfusions administered promptly were considered life-saving, and so it was only a question of how many transfusions a patient should get. Recently, on the basis of a five year survey, many eminent men have come to feel that the results with multiple transfusions are not as good as have been reputed.

A patient with massive hemorrhage should get 1000 cc. of blood, and this could be carried to 1500 or 2000; but beyond that, one is already doing a replacement of blood transfusion, which is hazardous because of transfusion reactions and for many other reasons. Rienhoff, in a recent editorial in the *Southern Medical Journal*, reported that platelets are depressed and that these patients develop ecchymoses.

## SURGERY

How can we decide how many transfusions a patient needs? Simple measures — hemoglobin, hematocrit, red cell count, blood pressure, pulse rate and perhaps blood urea nitrogen—are adequate. All of us are aware that changes as revealed by these measures do not follow quickly the loss of blood, and in many cases, the results may be misleading. But, if *all* of these five examinations are used frequently and accurately, they will form a satisfactory guide as to the patient's progress and the need for blood. A pulse rate which rises, from 80 to 90, to 100 to 110 or 120, shows that the hemorrhage is not under control; also a blood pressure which falls from 130 to 100, and perhaps to 90 or 80, indicates that this patient is losing ground. When the pulse rate is going up and the blood pressure is coming down, conservative measures must be abandoned. Blood is not controlling the situation, and surgery should be consid-

ered. Evidence afforded by other measures named will have the same trend. Only when the general condition is improved, the pulse rate is decreased, and the blood pressure and the amount of blood are on the upward trend, can we be sure that the patient is out of danger and that the hemorrhage has ceased. All this must take place in 48 hours. If the period is prolonged to 72 hours, then the best time for operation may have been lost.

There are other factors to be considered in deciding whether a patient is medical or surgical. If the patient is above 40, his vessels are or are *beginning to be* arteriosclerotic. Then perhaps one would take less chances with a hemorrhage which seems to be continuing. If a hemorrhage is brought under control only to recur, or if a hemorrhage is stabilized but not quite well enough, or if the bleeding is rapid, the patient may require surgery. In giving blood, one is not only trying to stabilize the patient but may be getting him into condition for surgery.

## DIAGNOSIS

There is a trend toward immediate diagnosis. In some clinics, the patient in severe hemorrhage (unless he is in shock) will be subjected to esophagoscopy, gastroscopy and X-ray within the first two hours. I am not one who belongs to this school of thought, and I have always objected. For example, when a resident calls in, all excited and says that "a patient is bleeding badly, will some one come and do an esophagoscopy and gastroscopy so that the surgeon will know where to operate?" The value to the surgeon of knowledge where the bleeding comes from is conceded. But, if one will analyse the situation, he is far better off than he believes. We know that 7 out of 10 massive upper gastrointestinal hemorrhages occur from ulcer, that duodenal ulcer must account for most; adding gastric carcinoma, gastritis and esophageal varices, he can account for 90% of the cases of bleeding. The incision for gastric carcinoma, for ulcer and for gastritis is very similar. Therefore, it becomes important only to decide whether esophageal varices are present. Also, early X-ray examination may disclose an ulcer or carcinoma. In recent years, the appearance of gastric varices in the absence of esophageal varices has been impressive.

## CLINICAL APPROACH

A barrage of endoscopic procedures and X-ray is not routine in most clinics. There are not many who can perform these procedures capably; also these procedures are not without their dangers, and a good clinical approach may be just as valuable. It should be routine in any massive gastrointestinal hemorrhage, not only to measure the degree of hemorrhage, but also to do a few liver function tests. From 2% to 25% of cases of cirrhosis may be associated with ulcer, and a positive bromsulphalein test, for example, points to varices rather than ulcer; vice versa for a negative test.

Some years ago, everyone did the gastrointestinal series after about two weeks—a safe period—after hemorrhage had ceased. Now, due to the introduction of the non-manipulatory method, these X-rays have been done during the period of hemorrhage, and a greater percentage of positive X-rays has been the

result. However, many radiologists prefer to do their X-rays with manipulation later on, and only in a few clinics do they favor very early examinations. Shortly after hemorrhage ceases, one can do an X-ray and find out what is going on. Sometimes in an X-ray two and three months after the bleeding, the scar will indicate the area the bleeding came from.

There is a group of 5% to 20% of patients in whom the cause for bleeding cannot be determined. If one takes time to talk to these patients, if they are not too sick, an ulcer history, or a history of alcoholism, will be helpful in pointing to the source of the bleeding. Any story of irregular or sudden onset of indigestion, or later anemia and loss of weight, causes one to consider gastric carcinoma.

A physical examination during a period of hemorrhage should be limited to blood pressure, pulse rate, rigidity of the abdomen, and whether the liver is palpable. Endoscopic and X-ray procedures should be considered very carefully since they can be traumatic.

## SUBTOTAL GASTRECTOMY

If it is known that there is a lesion, it can be eradicated; but what if a lesion is not known? A blind subtotal gastrectomy is now considered to be the best one can do for a bleeding patient when the cause is not known. It removes the acid-bearing tissue and takes care of the ulcer tendency. If there is a carcinoma, certainly that would be removed and removal of this vascular bed would reduce esophageal varices at least during the period of emergency.

There is a group of bleeders in whom a *possible* cause of bleeding is demonstrable, but at operation bleeding is found to come from another area. In a recent patient, a leiomyosarcoma was the cause of bleeding; the ulcer was there but it was not bleeding at all. In these cases should the non-bleeding area also be removed? That is left to the judgment of the surgeon.

Then there are bleeders in whom a cause for the bleeding is found but does not seem adequate; e.g., an atrophic gastritis. In another group, no cause for bleeding can be found. In some people with hypertension there may be vicarious bleeding from the gastrointestinal tract. In these patients when the cause for bleeding cannot be found, and especially those controlled by medical measures, repeated hospitalizations and examinations of every kind, and an occasional operation during the period of bleeding, should disclose the sources of bleeding in many cases.

In bleeding from esophageal varices, the emergency treatment is tamponade, done by a tube such as the Sendstaken tube. It may be lifesaving. There are surgeons who go in and do a transfixion of the bleeding esophageal varices. Definitive therapy for bleeding esophageal varices is the portacaval or splenorenal shunt. More and more younger men are doing these operations successfully. We know how to select our cases better. The operation is done primarily for bleeding and not for ascites or for improving liver function, although there is evidence these are being improved.

Reprints of this article may be obtained from S. Morrison, M.D., 11 East Chase St., Baltimore 2, Maryland.

# The General Practitioner's Part in Planning for Radiation Therapy

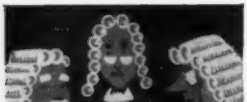
*Many difficulties which are experienced by the radiologist may be avoided by cooperation and consultation with the family physician*

FREDERICK B. MANDEVILLE, M.D., *Richmond, Virginia*

Once the mandatory complete clinical diagnosis, x-ray examinations, and pathological examinations have been established, and the consulting specialists have agreed that radiation therapy is in the best interests of the patient, the planning for the therapy should be made. It is here, before the patient is given the word of the plan, that the G.P. should be consulted and should assume a major role.

As the radiologist of tumor boards for 30 years, I have had the experience of seeing patients and families told of the need for radiation therapy for a specified period, e.g., 50 daily treatments, although conditions were such that such a plan could not be carried through. The G.P. should be consulted before the patient is told the plan of treatment (before the plan is made). He knows conditions and can evaluate possibilities.

An experienced radiologist, in some cases can give a single massive dose instead of daily doses over a long period, for example, in basal-cell epithelioma. He can time fractional doses for keloids at 2-, 4-, or 6-week periods. Daily treatments can be given on alternate days or on longer time schedules when trans-



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| (equivalent to 50 mg. ascorbic acid) | |
| Calcium carbonate . . . . . | 60 mg. |

* U.S. Pat. 2,691,662


1. Bunse, E.A.: Treatment of Rheumatoid Arthritis by a Combination of Cortisone and Salicylates. Clinical Med. 11:1105 (Nov., 1955).
2. Rosham, J., VanCawenberge, H.: Abst. in J.A.M.A., 151:248 (1953).
3. Coventry, M.D.: Proc. Staff Meet., Mayo Clinic, 29:60 (1954).
4. Holt, K.S., et al.: Lancet, 2:1144 (1954).
5. Spies, T.D., et al.: J.A.M.A., 159:645 (Oct. 15, 1955).



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portation conditions demand a change. The size and shape and number of treatment portals, the quantity and quality of roentgen and radium treatments should be varied to suit individual needs.

The equanimity of the patient is upset if he is presented with a rigid treatment schedule, and severe radiation sickness, or skin or mucosal reactions necessitate changes in the original plan. At the very outset of a series of treatments, the radiologist should allow leeway in mentioning his plan, and make no promises. He should quite frankly consider radiation sickness and unexpected reactions in his conferences with the patient, the family physician, the family, the social worker and public health nurse.

In all the malignant lymphomas and chronic leukemias and even in carcinomas in which later palliation can be obtained by further x-ray, radium or isotope therapy, the radiologist should broach possible plans for periodic checkups and additional future therapy to guard against discouragement and minimize it for the coming events.

The margin of safety in x-ray therapy is always less for benign lesions than for malignant ones. There are a whole series of embarrassing situations into which famous teachers of radiology have got themselves by multiple, continued treatment of benign lesions, most often on the foot or palm, of famous persons who came seeking cures. I have trained two residents in radiology whose own fathers, both radiologists, had over-treated them. G.P.s could help greatly by not re-referring to radiologists lesions which have been given a fair trial but have failed to benefit; and the G.P. should furnish the radiologist with information about all previous irradiation, cauterization and physiotherapy of all kinds, especially recent. He should consult with the radiologist and cooperate with him in making the patient avoid all hot and cold applications, alcohol, and all irritating solutions, ointments and dressings preceding, during and after radiation therapy.

The avoidance always, at all times, of the word "burn" is a must. First and 2nd degree radiation reactions of the skin and mucous membrane structures are necessary and expected, and the radiologist should always be given the opportunity to see them. For the weeks during and following therapy the G.P. should intelligently plan and prescribe medication internally as well as sedatives for pain and discomfort and to afford needed rest and adequate sleep. Fluid and dietary requirements within the bounds of the situation at hand can best be guided by the G.P. with the advice and cooperation of his radiologist.

*Mississippi Valley M. J.*, 77:193-194, 1955.

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1. Rehfuss, M. E.: Indigestion, Philadelphia, W. B. Saunders Co., 1943, p. 322.
2. Shaftel, H. E.: J. Am. Geriatrics Soc. *1*:549 (Aug.) 1953.

# Protrusion or Rupture of the Lumbar Intervertebral Disks

*When non-operative management brings good results; and indications that make it mandatory to use surgical procedures*

JAMES PETER MURPHY, M.D., *Washington, D. C.*

Protrusion or rupture of lumbar intervertebral disks is the principal cause of intractable pain in the back and leg.

The typical sequence of events with lumbar disk protrusion is:

1. Initial trauma to the lumbar spine, direct or indirect, remembered or forgotten.
2. Lumbago—the low back syndrome.
3. Sudden or gradual development of pain radiating from sacroiliac joint, hip and buttock to the lateral and posterior thigh, calf, ankle and foot.
4. Accentuation of symptoms with repeated back strains, severe or minor.
5. Eventual intractability of discomfort; sciatica outweighing pain in the back. The youngest patient in author's series was a 15-year-old girl, the oldest a man of 76.

Most patients with disk protrusion prefer a straight chair, avoid stairs and stepping off street curbs, and acquire many other habits to seek relief. Almost every one is made comfortable by lying flat on a hard surface, a bedboard or even the floor, and is made worse by standing or walking for long periods.

Exactly the opposite is true of the

patient with an intraspinal tumor. The patient walks with great care, bearing his weight on his "good" leg. He is bent forward slightly as his pelvis and hip are tilted up on the affected side, the painful leg slightly flexed to take stretch from the sciatic nerve. Compensatory tilting of the upper back and neck often causes pain in the neck, shoulder and arm. If the process is of long standing, there may be atrophy of the buttock, thigh and calf of the painful leg. The lumbar muscles are in spasm on one or both sides, and the lumbar spine is curved, usually with concavity toward the side of pain.

### DIAGNOSTIC AIDS

The diagnosis of protruded or ruptured lumbar intervertebral disk may be made when:

1. Low back pain occurs acutely or develops gradually after direct or indirect trauma to the lumbo-sacral spine.

2. Sciatic pain in the leg follows or accompanies back pain within a short period of time.

3. Pain is accentuated by walking bending, lifting, standing or sitting and is relieved by lying flat.

4. Limitation of flexion and extension of the spine, sciatic pain in the affected leg during straight leg-raising, and tenderness over a vertebral spinous process, lamina, and along the course of the sciatic nerve.

5. Sensory loss, reflex depression and motor weakness in the cutaneous and muscular tissues innervated by a specific lumbar or sacral nerve root or roots. Plain x-ray films of the lumbosacral spine may or may not demonstrate disk narrowing or arthritis and eliminate the possibility of cancer. Myelography in the majority of cases reveals external encroachment upon the lower dural canal as a filling defect in the vicinity of one or more nerve roots, usually at the fourth or fifth lumbar disk. Rarely a complete intraspinal block. The spinal fluid is clear.

### METASTASES

Lumbosacral neoplasms cause pain and neurologic changes in both legs, sphincters are involved frequently, relief is obtained by the erect posture or by walking, the spinal fluid is yellow, and myelography discloses a complete obstruction to the oil column or outlines the tumor. Metastatic cancer should always be thought of as a cause of low back pain, and sciatica in the elderly. Metastases may be in other bones or in the lungs; serum phosphatase values may be elevated; local destruction of the lumbosacral spine may be evident in plain x-ray films, and myelograph demonstrate multiple bilateral encroachments upon the dural sac by epidural cancer or vertebral collapse. Primary malignant tumors of bone in the lumbosacral spine or pelvis ultimately produce erosion, recognizable by x-ray.

Arthritic, sciatica, clinical and x-ray evidences of arthritis are evident. If myelography discloses a filling defect and nerve encroachment corresponds to complaints, disk rupture may coincide and nerve-root decompression from bony spurs may afford relief.

Marie-Strumpell's arthritis can cause severe sciatica in young people. Hypertrophic changes are seen in x-ray films of the sacroiliac joints, chest expansion is limited, and gritty ligaments are found at operation.

The not uncommon syndrome of enlarged epidural venous varices of the lumbar spinal canal cannot be distinguished from protruded lumbar disk disease, on either clinical or myelographic grounds. Sciatica is severe in the upright position, is relieved by lying flat, and back pain is usually minimal. The necessity of accurate preoperative distinction is of little concern, since patients with severe complaints must be treated surgically in either case and the unroofing of the intervertebral foramen to allow expansion of bulging veins affords the same relief as excision of a ruptured disk.

Nonoperative management is usually successful when:

1. The attack of low back pain and/or sciatica is an initial episode and has not lasted longer than 6 weeks.

2. The syndrome although of recurrent type is maximum lumbago and minimum sciatica.

3. General and X-ray findings indicate arthritis as a very probable cause of complaints and the patient is past 50.

4. Loss of sensation, weakness and reflex abnormality in the lower extremity are minimal or absent.

## CONSERVATIVE MEASURES

When the patient is anxious to avoid surgery, a trial of conservative therapy is often indicated even when a disk is obviously ruptured, if only to demonstrate the futility of measures short of removal of the disk. Under these circumstances the patient should be made aware of the possibility of permanency of footdrop or of other neurologic disability if delay in surgery is insisted upon.

The conservative measure most effective is complete rest upon a hard mattress supported by boards, the patient flat on his back or in partial flexion, whichever is more comfortable. Traction on the affected lower extremity, on both legs, or on the pelvis is of additional benefit. Seven pounds of weight is usually applied to each leg.

Diathermy or other heat over the lower back tends to relax spastic muscles, as does mephenesin (Tolserol) which is helpful when anxiety and restlessness tend to aggravate muscle spasm; analgesics — aspirin-codeine compounds are effective.

Massage of the back muscles, quadriceps setting, and hamstring relaxation shorten convalescence. Many obtain some benefit by flexion-extension manipulations of the painful lower extremity and lower back.

## BRACES AND APPLIANCES

Support of the back by adhesive tape applied tightly, or the use of a back brace or a body cast is often helpful in the stage of acute back strain or during a convalescent period. Some persons subject to repeated attacks of lumbago keep a brace on hand to wear during the multiple episodes which do not progress to severe sciatica. If, however, relief of back discomfort and particularly of leg pain is only partial, is largely the result of temporary limitation of forward bending, depends entirely upon continued wearing of the brace, or severe pain recurs as soon as the appliance is discarded, the patient usually has a protruded or ruptured disk which must be treated surgically.

Intensive conservative treatment

should bring about definite relief in 7 to 14 days. Further immobilization of the patient or of his back when no significant results have appeared in this period of time merely postpones inevitable surgery. When sciatica is severe and the only medical suggestion is that of continuance of obviously ineffective nonsurgical therapy, the sufferer may become despondent and even aggressive in his desire to be free from unbearable pain.

*M. Ann. District of Columbia*, 6:277-286, 195[illegible].

### Evaluation of a Sustained Release Belladonna Preparation

Milligram for milligram, none of the substitutes equals atropine in physiological activity, and none is free of side effects. A new sustained release dosage form of belladonna alkaloids, Prydonnal Spansule Capsules®, was given 30 patients with various gastrointestinal complaints, 12 of proven peptic ulcer. Excellent results were obtained in 18; good results in 8; fair in 1; and poor in 3.

Night pain was controlled in 16 of 19 for whom it was a problem. Side effects: 4 instances of drowsiness, 1 of blurring of vision, and 2 of dry mouth occurred in 6 patients.

The preparation appeared to maintain effective therapeutic levels for from 8 to 10 hours following ingestion, to effectively control night pain in hypersecretors, and to produce fewer side effects than t.i.d. belladonna therapy.

Burness, S. H., *Amer. J. Dig. Dis.*, 22:111-114, 1955.


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# Backache During Pregnancy

*Hormonal fractions present during pregnancy are responsible for backaches which increase during activity and can be controlled by support and relaxation*

JACK WICKSTROM, M.D., *New Orleans, Louisiana*

Irrespective of its cause, back pain is increased in severity either as a result of pelvic congestion or psychogenic disturbances experienced during gestation. Congenital anomalies are prone to aggravation during the last trimester.

Neoplastic lesions, either primary or secondary in the spine, are stimulated by the increase of growth hormone during pregnancy. Other backaches aggravated by pregnancy are those of faulty body mechanics or pressure or traction on the spinal nerves passing through the pelvis.

The commonest cause of backache at all ages in both sexes is poor posture and consequent altered body mechanics. The alterations consist of relaxation of abdominal musculature, a pendulous abdomen, increased lordosis, and forward rotation of the pelvis. The ache appears in the second trimester as discomfort upon arising, increased as the day wears on and partially relieved by recumbency, with reassurance and a regimen of periods of rest coupled with exercise to relieve abdominal muscles and strengthen the pelvic rotators. During the first trimester all exercises are flexion exercises. Those which produce strain on the abdominal wall or increased intra-abdominal pressure are avoided.

Provide proper support while the patient is lying down and during ambulation. Make bed semifirm by

## Notes on Diagnosis and Management of "Dizziness"

# I. Vertigo

"Dizziness" should be considered the tangible symptom of a specific pathology.

Moderate vertigo, with a sense of motion and a whirling sensation, may be produced by infection, trauma or allergy of the external or middle ear. Examination of the ear will usually disclose the abnormality.

Severe vertigo, which will not permit the patient to stand and causes nausea and vomiting, indicates an irritation or destruction of the labyrinth. The specific condition may be

**1. The Rotation (swivel chair) Test.**

***The patient sits in a swivel chair with his eyes closed and his head on a level plane. The chair is turned through ten complete revolutions in twenty seconds. Stimulation of a normal labyrinth will cause nystagmus, past pointing of the arms and subjective vertigo.***

3. Bárány Pointing Test. *The patient points at a stationary object, first with his eyes open and then closed. A constant error in pointing (past pointing) with his eyes closed in the presence of vertigo indicates peripheral labyrinthine disease or an intracranial lesion.*

labyrinthine hydrops, an acute toxic infection, hemorrhage or venospasm of the labyrinth or a fracture of the labyrinth. Multiple sclerosis and a pathology of the brain stem should be considered also.

2. The Caloric (Bárány) Test.

*The patient sits with his eyes fixed on a stationary object and the external ear canal is irrigated with hot (110 to 120 F.) or cold (68 F.) water. If the vestibular nerve or labyrinth is destroyed, nystagmus is not produced on testing the diseased side.*

It is important to learn if the patient's sensation is continuous or paroxysmal.[2] Paroxysmal vertigo suggests specific conditions: Ménière's syndrome, cardiac disease and epilepsy. Continuous vertigo without a pattern may be due to severe anemia, posterior fossa tumor or eye muscle imbalance.

Dramamine® has been found invaluable in many of these conditions. In mild or moderate vertigo it often allows the patient to remain ambulatory. A most satisfactory treatment regimen for severe "dizziness" is bed rest, mild sedation and the regular administration of Dramamine.

Dramamine is also a standard for the management of motion sickness, is useful for relief of nausea and vomiting of radiation sickness, eye surgery and fenestration procedures.

Dramamine (brand of dimenhydrinate) is supplied in tablets (50 mg.) and liquid (12.5 mg. in each 4 cc.). G. D. Searle & Co., Research in the Service of Medicine.

1. Swartout, R., III, and Gunther, K.: "Dizziness": Vertigo and Syncope, GP:*835* (Nov.) 1953.

2. DeWeese, D. D.: Symposium: Medical Management of Dizziness: The Importance of Accurate Diagnosis, Tr. Am. Acad. Ophth. *58*:694 (Sept.-Oct.) 1954.

SEARLE

placing plywood, fiber board or masonite between the mattress and spring. Some prefer the semiflexed position — a bedding roll beneath the knees to flex the hips and knees or the elevation of the lower leg on a chair while recumbent. A lumbosacral support which comes well down over the buttocks and supports the lower abdomen, affords significant relief.

Success is dependent upon complete cooperation of the patient.

Backache from pressure or traction on the spinal nerves in the pelvis, usually involves the ilio-femoral and ilio-inguinal, the sciatic or occasionally the sacral plexus. The recumbent position, or recumbency with elevation of the hips, or injecting painful trigger areas along the crest of the ilium may afford relief.

The backache unique to gestation is an endocrine balance resulting from certain hormonal fractions present only during pregnancy. It is held that hormonal relaxation of the pelvis accounts for a certain percent of symptoms in backache during pregnancy and that such backache is usually characterized by localization over the posterior iliac spine and over the symphysis pubis, increased with activity, and aggravated by pelvic distraction and compression. Usually a constricting support encircling the pelvis above the trochanters affords relief. Severe relaxation may require bed rest.

*J. Louisiana State M. Soc.*, 107:490-493, 1955.

## Eat Less Fat and Live Longer

During World War II in Norway and Finland, where there was forced reduction in dietary fats, there was a decrease in the incidence of coronary heart disease. With the end of hostilities and the return to a diet richer in fat content, the incidence returned to pre-war levels. Similar observations were made in Holland and Germany.

In Japan, a country whose diet is low in fat, hearts of 10,000 patients from all walks of life were studied. It was concluded that the incidence of coronary sclerosis in Japan is one-tenth that of the United States at all age levels. Only 75 deaths in this series of 10,000 autopsies were attributed to myocardial infarction.

In 1954, studies were made in Italy by Ancel Keys and Paul D. White of the populations of two cities — Naples and Bologna. The Neapolitans eat much less fat than the Bolognese; blood cholesterol concentrations are much higher in Bologna. Protein levels, average body weight and thickness of subcutaneous fat layer are the same in the two populations. The incidence of myocardial infarction and coronary heart disease is much higher in Bologna.

White compared the incidence of coronary heart disease among general ward admissions in Naples, Bologna, Massachusetts General Hospital and Malmo, Sweden. The percentages were 2.0, 18.2 and 16, respectively. In the twin cities of Minneapolis and St. Paul, the percentage is 26.2.

In the United States, diet fat made up 30% of total calories in 1910, and more than 40% in 1950. The mortality rate in this country from coronary heart disease is higher than in any other country.

Robbin, S. R., et al., *J. Mt. Sinai Hosp.*, 1:34-46, 1955.

# A New Approach to the Treatment of Functional Gastrointestinal Disorders

*This new anticholinergic preparation provides satisfactory relief of gastrointestinal spasm and serves as a diagnostic aid*

JOHN A. OLSON, M.D., *Cranford, New Jersey*

Many patients come complaining of gas, belching, bloating, heartburn, cramps, etc. Gastrointestinal x-rays usually reveal pylorospasm, and irritable duodenal cap, or a spastic colon. Many of the milder cases respond to dietary control, antacids, and "blocking" agents, but most are continuing problems with repeated changes in medication.

Perhaps a new approach to the problem of gastrointestinal spasm should be sought. A lead in this direction has been provided by Bradley, et al who observed that a pH adjusted phosphorated carbohydrate solution was effective in the control of epidemic vomiting in 172 children. Its antispasmodic effect on the human intestine was also apparent from the experience of others who report that this solution relieved the nausea and vomiting of early pregnancy in 78.8% of 123 patients. Its efficacy in other types of functional vomiting was observed in a series of industrial workers.

It was reasoned that if this topical action could be reinforced by addition of an anticholinergic blocking agent and phenobarbital, a very effective antispasmodic might result. So, homatropine methylbromide and phenobarbital were added to the

phosphorated carbohydrate solution, and the pH was adjusted to an optimal range. A clinical testing program was initiated using this combination, now available as Coactyn®.

It is a pleasant-tasting, apricot-flavored phosphorated carbohydrate solution containing phenobarbital, 8 mg., and homatropine methylbromide, 0.5 mg. per teaspoon. This solution was given to 120 patients with various gastrointestinal symptoms—heartburn, bloating, belching, gas, diarrhea, nausea, cramps and abdominal pain. Dosage was 1 or 2 teaspoonfuls undiluted 15 or 20 minutes before meals. If symptoms are not completely relieved, additional doses up to a total of 10 drams per day may be given. The instruction to administer it undiluted was emphasized since dilution lessens the topical spasmolytic action. The stomach being empty, direct contact with mucosal surface favors optimal effect.

Coactyn was administered in all cases in which gastrointestinal spasm was thought to play a part in the etiology. Ultimate diagnoses included functional spasm, pylorospasm, peptic ulcer, acute and chronic gastritis, gallbladder disease, spastic colitis, and carcinoma of the stomach or intestines.

Of 120 patients treated, 92 got satisfactory relief. These had varying types of functional gastrointestinal disturbances; 8 patients with peptic ulcer derived little benefit from it; 3 with cancer were not helped; 6 objected to the consistency and sweet taste and refused to take it; 11 others obtained better results from other anticholinergics in combination with larger doses of phenobarbital.

Patients complaining especially of heartburn, gas and epigastric discomfort stated that they could feel the distress "melt away" as soon as the liquid was swallowed. Those with bloating and severe abdominal distention were readily relieved. The immediate effectiveness must be attributed to the topical antispasmodic activity of the pH-adjusted carbohydrate vehicle.

Almost all patients who did not obtain relief were found on x-ray examination to have organic lesions such as: peptic ulcer, gallbladder disease, or gastric or intestinal neoplasms. This observation led to its consideration as a useful diagnostic tool in differentiating organic from functional GI disorders. If relief did not ensue after a 5-day trial, the patients were routinely subjected to further diagnostic studies.

*Coactyn, Kinney & Company, Inc., Columbus, Ind.

*Amer. J. Digest. Dis.*, 22:319-321, 1955.

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## Carcinoma of the Thyroid Gland

Carcinoma of the thyroid gland comprises 1% of all malignant tumors. This review of 219 cases of goiter, operated on during the period 1949-1953, includes 16 malignant tumors.

The incidence of malignancy has averaged 10% in the reports issued by large thyroid clinics. The general operative mortality is less than 1%. Most cancers of the thyroid are of low grade, and in most cases, early removal of the affected lobe will effect a cure.

Blackstone, M. A., *J. Iowa M. Soc.*, 45:73-74, 1955.

# Premenstrual Syndrome

*Treatment of this endocrinal disorder by progesterone brought relief to a large majority of patients; case histories are presented*

KATHARINA DALTON, M.D., *London, England*

Premenstrual syndrome is usually characterized by depression, irritability and lethargy. It should be suspected in a patient who has boundless energy one day, followed by a few days of lethargy and listlessness. Another guide is facial pallor and puffiness suggestive of anemia during an attack, but accompanied by good color of the mucous membrane and normal hemoglobin. Spontaneous bruising has been noticed; it is painless, bilateral and usually in more or less the same area, with common sites on the thighs and upper arms. Signs which may be noticed on day-to-day observations are weight gain, edema, albuminuria and hypertension. A weight gain and loss of over two pounds in a cycle is significant.

In common with many endocrinal disorders, the onset often comes with puberty, childbirth or menopause. At times of stress symptoms become unbearable; under favorable conditions, the symptoms decrease or pass by unnoticed.

Over the years the pattern of attacks may alter or symptoms change, e.g., rhinitis replaces asthma, or migraine replaces or is replaced by epilepsy.

Most cases end with the natural menopause, but an increase of symtoms is common at times of the first missed periods. Others continue with monthly attacks during their

sixth and seventh decades. A woman, 64 years of age, had monthly attacks of blackouts and vertigo, which were relieved by ethisterone; and another, 70 years of age, had regular attacks of asthma also relieved by ethisterone. A patient, 63 years of age, who developed eclampsia with her fifth pregnancy 26 years ago; had since had attacks of epileptic fits every month, and after a natural menopause at the age of 52, these attacks occurred every fortnight. After suffering epilepsy for 26 years, she was treated with ethisterone, 150 mg. daily, and has had no fit for the past two years.

It is too early to say whether remissions following a course of progesterone are permanent. A woman with severe premenstrual asthma has now had a remission of six years; at times of stress there is likely to be a recurrence.

Although other treatments of premenstrual syndrome have been tried, I always return to progesterone for consistently good results.

From a group of 78 cases treated with progesterone or ethisterone, 47.9 cases had complete relief following ethisterone and a further 17.4% improved. Progesterone gave complete relief in 83.5% and improvement in 6.6%; with increased dosage this "6.6%" might have become free from symptoms.

### ADJUSTMENT OF DOSAGE

Progesterone must be administered by deep intramuscular injections. It can be obtained in oily or aqueous suspension, given daily or on alternate days. Signs of overdosage are euphoria, insomnia, restless energy, dysmenorrhea (which in toxemia may resemble false labor pains), faintness and possibly hysteria. Occasionally urticarial weals and deep muscular tenderness follow an injection. Dosage may commence with 25 mg. on alternate days, but if this does not give complete relief the dose is given daily, and if necessary, a larger dosage may be used. The usual course is from the fourteenth to the twenty-sixth day, but if ovulatory symptoms are present, if there is weight gain before the 14th day, or if a postponed attack of symptoms occurs during or after menstruation, then the injections are continued throughout the cycle.

With marked water retention, less progesterone will be required, if urea or ammonium chloride is used daily or if mersalyl is given twice or thrice weekly (can be given in the same syringe as progesterone.) While this provides less expensive treatment, dehydration alone rarely brings that complete relief of all symptoms and that sense of well being which is such a feature of progesterone therapy.

### ACUTE ATTACKS

Although progesterone should be used before the onset of symptoms, an acute attack of asthma, migraine, psychosis, epilepsy, or depression often can be cut short by the simultaneous injection of 50-100 mg. progesterone and mersalyl 2 cc. This may be of academic interest only in regard to some symptoms which respond equally well to other methods —e.g., adrenaline in asthma—but some acute cases of migraine, psychosis, and depression can be relieved in four to five hours with this double injection.

Progesterone therapy of premenstrual syndrome has been a new and so far successful, therapeutic ap-

**Arithmetic, algebra, and geometry are not the only sources of figure problems for the teen-age girl.**

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proach to the treatment of toxemia of pregnancy. During pregnancy a test dose of 25-50 mg. progesterone is given if any symptoms develop. If this dosage removes the symptom, that symptom is regarded as a possible early sign of toxemia. Continuous treatment with progesterone is then instituted; and if symptoms later recur, the dosage of progesterone is raised until the patient again is free of symptoms.

### CASE HISTORIES

Case histories include a patient 25 years of age, gravida 3, who received progesterone for premenstrual hemicranial headaches and lethargy following her second pregnancy. At 28 weeks of her third pregnancy, she complained of hemicranial headaches and bloatedness. She had gained sixteen pounds in the previous four weeks and her blood pressure was 145/90. The test dose of 25 mg. progesterone relieved the headache for 48 hours, but then the headache returned. She was then treated with 25 mg. progesterone on alternate days. Her blood pressure fell, weight gain decreased, and there was no recurrence of headache. She had a normal spontaneous delivery at full term.

Another case concerns a patient who was hospitalized at 34 weeks for toxemia during her first pregnancy. After two weeks' bed rest, she had a surgical induction, developed uterine inertia in the first stage of labor and later had a high forceps delivery. In her second pregnancy, she complained of headache, spots before her eyes and nausea at 27 weeks, no toxemic signs, but the test dose of 25 mg. progesterone brought relief from all symptoms for 24 hours. She was, therefore, treated with 25 mg. progesterone daily. At 30 weeks she had a recurrence of headaches, but still no toxemic signs. When the dose of progesterone was raised to 50 mg., all symptoms again disappeared. At 34 weeks, she had severe headache, vomiting, and spots before her eyes. It was a Monday, and the patient explained she always felt bad on Mondays as the district nurse, who gave the daily injections, did not come on Saturdays or Sundays.

At this time the patient had edema of ankles and face, albuminuria and blood pressure of 180/100. She was treated with 150 mg. progesterone and 2 cc. mersalyl immediately; the following day she felt better, the blood pressure had dropped and albumin disappeared, but the edema was worse. This disappeared by the third day. She remained on large doses of progesterone and continued to improve, and she was ambulant throughout. At 36 weeks she developed a large urticarial weal at the injection site. As she had been free from symptoms for almost two weeks, the injections were stopped for one day, but on the second day there was a recurrence of headache, vomiting and epistaxis with hypertension, but no edema. Daily injections again made her symptom-free. She had a normal spontaneous delivery at full term.

*Proc. Roy. Soc. Med.*, 5:339-347, 1955.

# Acute Disease of Abdominal Organs in the Aged

*Elderly people will withstand operation remarkably well if there is no undue delay and minimal intervention is carried out*

A. STANDEVEN, M.D. and M. CHIR, M.D., *Brighton, England*

This paper reviews 120 personal cases of acute abdominal emergency, excluding acute retention of urine, in patients over the age of 70. This series is a consecutive one, and no case, however unpromising it appeared on admission, has been excluded. The mortality rate includes all patients who died in hospital; and all survivors were ambulant on discharge.

Intestinal obstruction, by far the commonest acute surgical condition in old age, bears a heavy mortality. Age *per se* does not influence the mortality in operations for acute abdominal emergencies in the elderly. The total mortality of 26.7% is virtually the same as that of the other series reported.

Interesting features here were the high incidence of femoral hernia in old men, and the finding of the vermiform appendix, strangulated and gangrenous, in one femoral and two inguinal sacs. One femoral hernia was diagnosed only at laparotomy for small intestinal obstruction, when a loop of bowel was found just entering the femoral canal on the left side, as a Richter's hernia. Even knowing it to be present, and under full anesthesia, it was still not possible to feel this hernia through the fat of the groin. Richter's hernia was, in fact, very common in the femoral cases.

Half of these hernia cases were

admitted to hospital 24 hours or less after the onset of strangulation. In cases of Richter's hernia, the delay in admission was 7 days in one case, 6 days in 3, 5 days in 3, and 4 days in 2 cases.

### CARCINOMA OF THE COLON

Among other causes of obstruction, the largest single cause was carcinoma of the colon. Surprisingly, adhesions were responsible in an equal number, for the two cases of small-gut volvulus and were due primarily to adhesions. The cause of the adhesions was post-operative in 8 cases and a calcified tuberculous mesenteric gland in one; no cause could be traced in the remainder.

The average length of history was 3½ days in small-gut obstruction; 4½ days in the large-gut cases—suggesting both the complacency of the patient before seeking medical aid and the difficulty in diagnosing the mechanical obstruction.

Of the 13 deaths the abdominal condition was directly responsible for the fatal issue in 7 cases and indirectly so in one (pulmonary embolism). Two patients died from congestive heart failure, present on admission; 2 more died of cerebral thrombosis; and the 13th case, of hemorrhagic cystitis due to a self-retaining catheter employed for incontinence of urine. One patient with perforation of the colon above a carcinoma survived after laparotomy, colostomy, and drainage of the area.

### PERFORATED PEPTIC ULCER

There were 7 cases of perforated peptic ulcer (6 duodenal, 1 gastric), with one death on the 4th postoperative day. In this case the liver was found to be replaced almost completely by deposits of carcinoma. The primary growth showed in the bronchus at postmortem with no gross pulmonary collapse. The other 6 patients made uneventful recoveries and were all well when seen later as out-patients.

One old man, operated on in 1942, at 80, had had operations in 1945 and 1948 for perforated duodenal ulcer and had survived a hematemesis in 1949. At operation most of the anterior wall of the proximal duodenum was found to have sloughed, leaving a hole 3 by 7 cm. This was closed by suture, and a posterior gastrojejunostomy performed. He was readmitted in 1954 with severe abdominal pain, otherwise hale and hearty. His symptoms quickly subsided, and a barium meal showed the gastro-jejunostomy to be functioning, with no evidence of anastomic ulcer. The stomach was also emptying in part through the pylorus.

Three of these patients were seriously ill on admission, with grunting respiration, cyanosis; and rapid, low-pressure pulse. On operation it was remarkable how the respiration and the heart improved at once when the abdomen was opened and the irritant fluid sucked out. None gave rise to any further anxiety.

### APPENDICITIS

Acute appendicitis, 15 cases, all treated by operation, with 3 deaths. In 10 cases the appendix was gangrenous and in 6 diffuse peritonitis was present; 10 of these cases were diagnosed correctly and sent to hospital within 48 hours of onset. In only one case was diagnosis unduly delayed. A woman of 83 admitted on the 7th day of symptoms with obvious diffuse peritonitis, had epigastric pain for 7 days and had vomited

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**References:** (1) Bruce, D. D.: J. Nerv. & Ment. Dis. *121*:67, 1955. (2) Koppanyi, T.; Morgan, C. F., and Princiotto, J. V.: J. Am. Pharm. A. (Scient. Ed.) *44*:221, 1955. (3) Fazekas, J. F., and Koppanyi, T.: To be published. (4) Steininger, E.: Prakt. Arzt *7*:224, 1953.

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once daily for 6 days. The 2nd death was due to bronchopneumonia on the 13th day, the 3rd from peritonitis on the 3rd day. The appendix had sloughed and the pelvis contained fluid feces.

In none of the 5 sigmoid perforations, was the cause of the perforation identified with certainty. There was no evidence of carcinoma, and presumably a diverticulitis or stercoral ulcer was the initial lesion.

## ELDERLY PATIENTS

In the accurate diagnosis of acute abdominal disease, a clear and chronological account of the symptoms is of the utmost value, and it is just this information which is most difficult to obtain from old people. It is well worth while to take a history from one who has been nursing the patient. These patients appear much less sensitive to pain than the average adult. The tendency among the elderly to attribute any abdominal pain to "indigestion" or to constipation leads to delay in seeking advice. Abdominal signs are nearly always present, and can usually lead to the correct diagnosis. In peritonitis one cannot expect the same degree of rigidity in an old lady as in a muscular young man. Vomiting is not invariable with hernia of the Richter type.

The diagnosis of mechanical obstruction can be extremely difficult, particularly in cases of carcinoma of the colon, where acute is superimposed on chronic obstruction. Vomiting tends to be less in the elderly.

Of the 7 perforated peptic ulcer cases, 4 presented the typical clinical features, 3 patients complained only of sudden severe pain in the right iliac fossa.

## SURGERY IN THE AGED

Operation in these old people should not be delayed for more than an hour or two for resuscitation and correction of fluid balance. These patients are tougher than they look and withstand operation well, provided it is performed quickly, and only the minimum necessary is done. Not one of these patients was considered unfit for operation, and local analgesia was used for only 3 of those with strangulated hernia. All others were anesthetized with cyclopropane, with or without a relaxant drug.

In the strangulated herniae, areas of bowel, gangrenous or of doubtful viability, were invaginated where possible, in preference to resection. This is quicker and safer and is not followed by obstruction due to stricture.

For intestinal obstruction a laparotomy was performed rather than a blind decompression operation. A cecostomy causes so much distress to old people that it can rarely be justified as a blind or as a planned procedure. The future is short for these patients, and we should make this future as comfortable as possible rather than perform lengthier procedures of academic accuracy.

Old people are intolerant of intragastric tubes, and in such cases there is less upset to the patient in the postoperative period if the tube is passed twice a day and removed as soon as the aspiration is completed. This may not be as efficient as continuous suction, but the results are better, owing to the greater mental and therefore physical rest of the patient.

The perforated peptic ulcers were treated by early operation, closure

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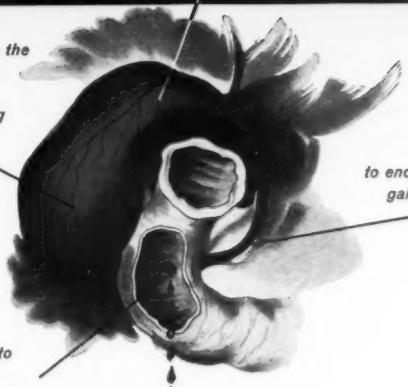

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of the perforation, and removal by suction of all fluid from the peritoneal cavity. It is surprising how much can be thus removed from the pelvis and from above the liver —2 pints is not unusual—and amazing to see the improvement. Drainage of the operative area or pelvis was not employed in any of these cases and there were no complications.

*British M. J.*, 4949:1184-1187, 1955.

## Management of Advanced Cancer

The belief that cancer of the breast and of the prostate are often not autonomous tumors but hormone-dependent has led to the remote control of disseminated mammary and ovarian cancer by gonadectomy, adrenalectomy or hypophysectomy.

Neurosurgical control of pain by local section of nerves, cordotomy, and leucotomy has a useful place in the management of severe pain in a small group of patients. A wide group of malignant tumors in an advanced stage can be temporarily controlled by a variety of radiotherapeutic measures. Artificial radioactive substances are replacing x-rays and radium as cobalt and caesium become available.

The most commonly used isotopes are those of iodine in the treatment of metastases from thyroid carcinoma, radioactive gold by injection into the pleural or peritoneal cavities in some cases of malignant pleural effusion or ascites and radioactive phosphorus, in the management of polycythaemia and in a few terminal cases of lymphosarcoma.

Nitrogen mustard is of great palliative value in the late stages of Hodgkin's disease. Remissions are obtained even when the liver and spleen are grossly enlarged, in the presence of continued or intermittent fever and when widespread lymph-node enlargement no longer responds to radiotherapy. *Oral* nitrogen mustard has given encouraging results as maintenance therapy following a course of *injections* of nitrogen mustard. The oral substance has also proved of value in multiple myeloma either alone or in combination with estrogens, and it has a retarding effect on disseminated malignant melanoma. Myleran (Haddow) has given palliation in chronic myeloid leukemia for periods up to two years and is so far the only substance which can be considered as a substitute for radiotherapy.

Estrogens are useful in cancer of the prostate and in cancer of the breast in women, well past the menopause, but not in men. Androgens are of value in mammary cancer in women, but not in men. Both androgens and estrogens can produce regression of the primary growth and of metastasis both visceral and skeletal. In many patients, the tumors, at first dependent, become hormone resistant.

In the terminal stages of cancer, morphine and its derivatives remain the most important pain relieving drugs. Skeletal pain can be relieved by X-ray therapy. Uncontrollable pain from involvement of nerves can be achieved by injections of nerves, cordotomy or leucotomy. Morphine and its derivatives should remain the last resort, and their function then is to help the patient to die.

Cade, S., *Proc. Roy. Soc. Med.*, 5:373-376, 1955.

# Investigation and Treatment of Septic Abortion

*Extensive observation of approximately a thousand cases solved many of the problems they presented and established a better prognosis*

A. MELVIN RAMSAY, M.D., *London, England*

Postpartum puerperal sepsis has now ceased to be a serious problem, and can usually be treated without removal of the patient to a special unit. Postabortum sepsis still presents diagnostic and therapeutic problems, and it is the purpose of this paper to review these in the light of our experiences of the past 5 years.

A fundamental difficulty in the classification of cases of septic abortion arises from the fact that the uterus is not always involved in the infective process. We have therefore classified the 995 cases occurring in the period under review into 3 groups:

1. Those with complete or incomplete abortion without uterine infection (421 cases).

2. Those with local uterine infection (482 cases).

3. Those with spread of infection to the uterine appendages, peritoneum, blood stream, or viscera (92 cases).

The common criteria of uterine sepsis comprise: (1) general signs of infection, of which fever and rapid pulse are the most important; (2) tenderness and subinvolution of the uterus and alterations in the lochia; and (3) bacteriological and hematological findings. None of these are in themselves indisputable evidence of uterine infection.

The organisms most commonly

found in puerperal infections:

1. Hemolytic streptococci of Lancefield Group A, invariably pathogenic.

2. Hemolytic streptococci of Lancefield groups other than A, nonhemolytic streptococci (mainly *Strep. faecalis* or *enterococcus*), coli forms, the 2 groups of anerobes — the sporing type represented by *Cl. welchii,* the non-sporing type by the anerobic streptococcus — and coagulase-positive staphylococci. These are usually saprophytes but are potential pathogens. The staphylococcus (small in incidence in this series) is apt to produce serious complications.

3. Coagulase-negative staphylococci and diphtheroids, purely commensals and we classify them as negative cultures.

### POST-ABORTION SEPSIS

The 6 organisms accounting for 98% of all pathogens — coliforms, C1. Welchii, non-hemolytic streptococci, anerobic streptococci, staphylococci, hemolytic streptococci — in post-abortum sepsis as opposed to postpartum sepsis:

1. Hemolytic streptococci of Lancefield Group A seldom found.

2. Bowel-derived organisms most commonly found (usually saprophytic, they require favorable factors for conversion to pathogenicity).

3. Mixed infections are common.

The management of a case of abortion depends on the stage at which it is seen, and on factors such as hemorrhage and infection. Occasional cases of threatened abortion or even of ruptured ectopic gestation are admitted with a diagnosis of septic abortion.

In Group 1, chemotherapy is not required unless removal of retained products is necessary. "Sulphatriad," 1.5 g., and penicillin, 250,000 units, are given q 6 h. for 5 days.

In Group 2, all cases require the combined course of sulfas and penicillin. Evacuation of retained products is delayed until the drugs have been given for 24 to 36 hours; excessive hemorrhage will demand immediate intervention.

In Group 3, blood cultures on admission should be routine. The commonest invasive complications were: salpingitis, parametritis, and spreading or localized peritonitis. Smaller collections of pus usually resolve; some drain spontaneously per rectum or per vaginam. Laparotomy for drainage has not been required during this period. Partial ileus may occur in cases showing tardy response to treatment.

### STAPHYLOCOCCI

The most gratifying feature of the past 5 years has been the virtual disappearance of severe staphylococcal infections. In view of the persistence with which these organisms develop resistance to each new antibiotic, it would be too much to expect no further trouble from them. The rapidly developing symptoms of acute *Cl. welchii* septicemia — jaundice, falling blood pressure and port-wine urine — are occasionally seen but prompt treatment with penicillin quickly arrests the infection. On occasion *Bact. coli* may give rise to a fulminant septicemia; in one of our cases death occurred within 24 hours of abortion, before chemotherapy had a chance.

Prompt treatment of a case of septic abortion with combined sulphonamide and penicillin controls most


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infections. Failure to respond usually indicates infection with coliform organisms or penicillin-resistant staphylococci. Since 1951 we have been impressed with the efficacy of chloramphenicol in this type of case.

Modern therapy has largely eliminated infection as a direct cause of death, and renal failure has now become the most dreaded complication of post-abortum sepsis. It was the cause of death in 2 of our 4 fatal cases; in the other 2 death occurred within 24 hours of admission and before chemotherapy could be effective. The prognosis now is favorable. Limitation of fluid intake and the non-protein diet have made this possible. We have found the fat content of the "Hammersmith cocktail" to be badly tolerated by many patients, and this may be halved without detracting from the value of the treatment.

*Brit. M. J.*, 4950:1239-1243, 1955.

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## Thrombosis of the Abdominal Aorta

Intermittent claudication is the cardinal symptom of slow arterial occlusion in the lower extremities. When the terminal aorta and iliac arteries are involved, this symptom is not the intermittent limp due to pain in the calf of the leg or foot, that usually results from functional hypoxia in the muscles of these parts. It is an aching sensation just short of pain and similar to the sensation of fatigue. It is typically located in the region of the hips and low back.

Leriche states there are two cardinal symptoms of aortoiliac thrombosis, loss of penile erection and extreme liability to fatigue of the lower limbs—a weariness rather than a pain—relieved by rest. In other groups of cases the number complaining of, or admitting, impotence was small.

The classical finding in this disease concerns the diminution or absence of pulsations in the arteries of the lower extremities—the femoral and iliac arteries, and the abdominal aorta. The absence of pulsations constitutes the greatest single important finding.

Chronic, insidious thrombosis of the abdominal aorta is probably more prevalent than the number of recognized cases would indicate.

Aortoiliac thrombosis often may be mistaken for an orthopedic or for a neurologic disturbance. The "hip-type" of claudication should direct attention to the possible presence of aortoiliac occlusion; and loss of arterial pulsation in the femoral arteries or abdominal aorta should confirm the diagnosis.

A long and active life is the outlook for many patients who have the chronic, insidious type of aortoiliac thrombosis. Occlusion of the renal arteries by cephalad extension is the greatest danger, and gangrene of any part of the lower extremities is the least of the probabilities.

So many get along well without surgical intervention that it should be reserved for the minority of cases who become greatly disabled.

Covey, G. W., *Nebraska M. J.*, 6:205-210, 1955.

# Bedside Considerations of Pituitary Disease

*Emphasis, in this classification of symptoms and therapy, is placed on hypothalmic alterations which may influence pituitary dysfunction*

THOMAS HODGE MCGAVACK, M.D., *New York, New York*

The classification of pituitary disease which follows is based solely on its usefulness in making an earlier diagnosis and in pointing the way to helpful therapy. In attempting such a classification, the proximity of the pituitary to vital neural structures and its physiologic integration with them cannot be ignored; hence, the emphasis is placed on the hypothalamic alterations which may be present with and influence pituitary dysfunction.

## PITUITARY LESIONS WITH FOCAL SYMPTOMS AND SIGNS

Of hypophyseal lesions, only tumors are associated with focal symptoms and signs, of which the most common are headaches, impairment of vision, and changes in the size and shape of the sella turcica. The headaches may vary from mild to severe and intractable. Vomiting and papilledema may later accompany the headaches, particularly if the tumor is large, or expands rapidly.

A bitemporal hemianopsia was present in 65% of Cushing's cases of pituitary tumor. Ballooning of the sella with erosion is almost pathognomonic of a hypophyseal tumor. This sign is virtually always present in cases of craniopharygioma, is commonly seen in both acidophilic and chromophobic adenomas, almost

never with tumors of the basophilic cells; rarely metastatic tumors and aneurysms give rise to similar changes.

Other manifestations of pituitary tumor are cavernous sinus syndrome, internal hydrocephalus, and evidences of hypothalamic dysfunction due to pressure. In its classic form the cavernous sinus syndrome consists of ptosis, convergent strabismus and dilation of the pupil, intense tic douloureux, congestion of the eyelids, and swelling of the veins of the face.

In one third of the chromophobic adenomas, there is no evidence of disturbance in endocrine function. In the remainder, suppression of such functions is associated with the displacement and final atrophy of many of the active endocrine types of cell.

### CRANIOPHARYNGIOMAS

Any intracellular tumor occupying sufficient space will eventually suppress the normal hormonal functions of the pituitary to a greater or lesser extent. Since basophilic adenomas are rarely much more than microscopic in size, they rarely cause disturbance of pituitary function as a *result of pressure*. Craniopharyngiomas, whether arising above or within the sella, almost always "crowd" the pituitary with diminution of secretory activity. The great majority of these tumors interfere with pituitary function before the end of the second decade, retard growth and sexual development. In patients with chromophobic adenomas gonadal function is disturbed in three quarters, adrenal function in one third, and thyroid activity in one fifth.

Suppression of pituitary function may similarly be seen as a result of large eosinophilic adenomas which are no longer actively secreting. By contrast the functionally active tumor of this type causes acromegaly in the adult and gigantism in the growing child.

### PITUITARY LESIONS WITH ENDOCRINE MANIFESTATIONS AND NO FOCAL SIGNS

These lesions may be divided into those with (1) increased, (2) decreased or with (3) one or more hormones increased and others decreased.

Hyperfunction of the eosinophilic cells of the anterior pituitary may give rise to *gigantism or acromegaly*, in rare instances without the formation of tumor. Very mild cases of this type can be recognized in everyday practice. Growth changes not shared by close relatives may be of value in treating a patient with overt diabetes mellitus, in correcting secondary gonadal disorders, and in preventing the subsequent appearance of more advanced aberrations in development.

The "transient" acromegaly of pregnancy usually occurs without any signs of tumor formation, but always leaves mild but unmistakable alterations in acral and soft tissues.

Pituitary basophilism with or without tumor rarely causes any focal symptoms or signs, but produces the characteristic Cushing's syndrome. A majority of observers are of the opinion that the changes in the adrenal are always or nearly always primary, the alterations in pituitary secondary. "Mixed" syndromes are not infrequently observed with or without evidence of local symptoms and signs.

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References: 1. Plunim, J. J., et al.: J.A.M.A. 157:931, 1955. 2. Forsham, P. H., et al.: Paper presented at First International Cong. on Prednisone and Prednisolone, New York, May 31-June 2, 1955. 3. Perlman, P. L., and Tyler, F. H.: Scientific Exhibit presented at A.M.A. Annual Meeting, Atlantic City, June 6-10, 1955.

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*brand of prednisolone

hyperfunction of the eosinophil cells, with its dramatic influence on general somatic development, may be followed by a return to normal or a decrease in the function of these cells.

In some instances one hormone or group of hormones suffer more than the others so that specific pituitary syndromes with secondary effects predominantly in the function of a single target organ may be identified. Pituitary myxedema is diagnosed by lack of the bodily habitus of primary myxedema, and by changes in adrenal function, poorly preserved gonadal activity, and altered responsiveness to the use of thyroid hormone — which must be used most cautiously. Here, too, may be placed at least two postpartum syndromes in which the pituitary does not recover fully from the normal gestational suppression: persistent lactation with or without ovarian and uterine atrophy and postpartum asthenia.

## HYPOTHALAMIC DISTURBANCES

Involvement of the hypothalamus, not uncommon in most types of pituitary tumors, is generally present in the nonpituitary extrasellar types of lesions. The latter may give rise to functional endocrine disturbances without any proved organic changes in the pituitary. Frohlich's syndrome is now believed to be primarily a disease of the hypothalamus. The alterations in water, fat, and electrolyte metabolism and the gonadal changes can be accounted for by the changes in the hypothalamic nerve centers. Any change in the pituitary or other glands is secondary. What used to be called "girdle" or "pituitary" obesity must be now recognized as hypothalamic in origin. The participation of the hypothalamus in premenstrual tension with water retention seems now to be established, the pituitary plays a secondary role.

## CLINICAL TESTS

Many of the tests are influenced by the activity of more than one gland so that considerable overlapping of usefulness occurs.

Urinary gonadotropins have their origin in the pituitary gland and should be a good index of at least one group of its functions. X-rays of the bones afford some information. Thyroid function can be appraised by the use of serum protein-bound iodine levels and cholesterol values, the basal metabolic rate, and radioactive iodine uptake. Gonadal activity influences thyroidal function, and a similar connection has been demonstrated between the thyroid and the adrenal cortex. These relationships are, at least in part, mediated through the pituitary so that the interpretation of any test must be made in the light of what these other glands are doing.

Gonadal function in the female can be assessed quite easily by serial vaginal smear. The most useful single test for adrenal insufficiency is the Kepler-Robinson-Power water test. The Soffer salt-tolerance test is the most helpful for Cushing's syndrome.

If all efforts at localization fail, it is best to consider the adrenal as the site of the primary lesion for, by operation of the law of chance alone, one will thus be right 99 out of 100 times.

## TREATMENT OF PITUITARY TUMORS

Rarely can the whole mass be re-

move l, and operative risk is such that less radical measures have found considerable favor.

*Ho monal therapy:* In the case of eosin philic adenomas, testosterone has h d suppressive effect on growth and metabolic disturbances. It shoul l be tried in all patients in whor vision is not at all or only sligh ly affected and in whom chan es in the visual fields are progress ng only slowly or not at all. Test sterone propionate in sesame oil, daily—100 to 200 mg. intramuscula ly for the first week, and 50 to 100 ng. for from 3 to 5 weeks longer, usually constitute a course of treat ment. For long-acting testosterone cyclo-pentyl propionate 200 mg. twice weekly for 4 to 6 weeks. Sometimes permanent relief follows a single course, or this may have to be repeated, rarely more often than yearly. Prompt regression of local and metabolic signs have been observed, with return to previous vocations without handicap.

*Roentgen irradiation:* Best results are in eosinophilic tumors with acromegaly; they usually run a benign course and are the most sensitive to x-radiation. The results of radiation are poorest when optic atrophy has occurred and the tumors are large: surgical procedures face the same handicap.

If no improvement within several weeks, surgical removal must be contemplated.

*Surgery:* The smaller the tumor and therefore the earlier it is removed, the less the surgical risk. All other measures should be tried before surgical intervention is attempted.

### PANHYPOPITUITARISM

It is necessary to substitute for the hormones of the target glands, diminished or absent due to the loss of pituitary hormone stimulation. The adrenal steroids must always be replaced to some extent in any instance of pituitary failure. Gonadal and thyroid replacement are also usually in order, the amount of each governed by the degree of impairment. Cortisone daily, 25 to 50 mg., is usually sufficient to supply the adrenal cortex deficit. Sometimes a small intraoral dose of desoxycortisone acetate is also advisable, particularly when hypotension is persistent. Testosterone makes the best gonadal therapy in both the male and the female. Daily intraoral doses, 5 to 10 mg. in the female, 10 to 30 mg. in the male. Desiccated thyroid daily 0.5 to 3 grains may be required, but it is best to delay the administration of both the gonadal and thyroid hormones for several days until the adrenal substitution has had an opportunity to improve the body's handling of carbohydrate and protein.

### TREATMENT OF HYPOTHALMIC DISTURBANCES WITH PITUITARY MANIFESTATIONS

When the obesity is of the familial lipodystrophic type, reduction in weight is difficult through dietary restriction. Most of the weight disappears from those areas which are already thinnest — the upper parts of the body, face and neck. In such cases diets which were intolerable become acceptable when moderate doses of cortisone are added to the regimen (20 to 50 mg. daily in divided doses); weight is lost from those parts which are heaviest. If the diet is faithfully followed in conjunction with the cortisone therapy, no untoward manifestations will appear,

and in the doses recommended added K is not required.

In the water-retention syndromes water retention is not related to the menstrual cycle, there is little to be gained from the use of ovarian hormones, and they may make the condition worse. Too great a restriction of carbohydrate or protein defeats its purpose. Less than 1,200 calories is inadvisable, but fat should be held to 40 gm. daily. Mercurial diuretics are contraindicated, despite the dramatic response. A gonadotropin made from pregnant mares' serum (Upjohn's Gonadogen or Cutter's Gonadin), given 3 times weekly for the first 2 weeks of each menstrual cycle or each month in the nonmenstruating person, in individual doses of 400 international units, will usually be effective.

If the water-retention syn rome is seen in conjunction with pr menstrual tension, moderate doses of estrogen and large doses of pro gesterone will be needed. In addit on, a diuretic of the theophylline se ies is useful. The most effective is I amabrom. When an antihistamine drug is added, the action seems to be enhanced. We have employed a mixture of Pamabrom and pyrila mine maleate (NeoBromth, Bray ten). Two tablets of this mixture, wice daily for 4 to 7 days before the menstrual flow, will usually be effective in preventing the retention of water and in relieving many of the undesirable features of the premenstrual tension syndrome.

*New York State J. Med.*, 55:3415-3421, 1955.

## Fructose Instead of Glucose

In the past few years, fructose has taken an important place in the management of ketosis and in surgery, etc. in diabetics requiring IV therapy. It seems clear that in diabetes the phosphorylation of glucose to glucose-6-phosphate (the first step in its metabolism) is impaired. In the absence or scarcity of insulin, the phosphorylation of fructose appears to proceed at its normal rate in the diabetic. In non-diabetic patients, postoperatively for example, this finding has practical application in that there is ⅔ less loss as glycosuria after fructose than after glucose. The diabetic in ketosis utilizes fructose at a normal rate without insulin, and the blood ketone levels fall more rapidly than with only saline. This latter is also true with glucose, but hyperglycemia is less prolonged, glycosuria is less and the rate of utilization is faster with fructose.

Important also is recognition of the importance of K and other electrolytes, and insulin and water.

Severe dyspnea due to respiratory muscle paralysis 21 hours after the start of routine treatment for acidosis. Serum K low, there was dramatic response to IV KCl. Although initial K levels may be normal, or even high, the deficit becomes apparent as hydration occurs, and there is a clinical picture of respiratory paralysis and vascular collapse. Prompt treatment is necessary, and is simple. Most often, a 10% solution of diabasic K phosphate is administered orally. Intravenous 1% KCl in water is rarely necessary. In either case, however, there must be an adequate urinary output before K is given.

McKay, Jr., R. V., *J. Iowa M. Soc.*, 11:560-56 1955.

# Case Record of the Massachusetts General Hospital Clinicopathological Exercises

*Symptoms included a gradually increasing hoarseness leading to paralysis and fixation of the left vocal cord and clubbed fingers*

---

A 52-year old man, in excellent health until last 3 months, when he began to feel "run down," lost appetite and over last 2½ months lost 10 pounds, entered hospital because of hoarseness. One month before entry a hacking cough began productive of small amounts of nonbloody sputum. There was gradual appearance of hoarseness, which increased up to admission. Examination of larynx revealed paralysis and fixation of the left vocal cord. A lateral x-ray film of the neck was negative. In hospital no difficulty in swallowing and no dyspnea, hemoptysis or pain in the chest. Had smoked 1 or 2 packages of cigarettes every day for many years.

Positive findings: Voice hoarse and rasping. Harsh late inspiratory wheeze in the right side. Marked clubbing of finger and toenails.

X-ray film of chest showed a round mass protruding into the left lung field just below the aortic arch, appeared to lie in the anterior mediastinum and showed slight pulsations. Lungs emphysematous with depression and flattening of diaphragm. A-P diameter of chest increased. Prominence of the left ventricle and the aortic arch. The mass moved with the aortic arch in a manner suggesting that it was fixed to it. An angiocardiogram revealed that the mass in the region of the left ductus node did not opacify as the dye went through the pulmonary vascular circuit and the

aorta. The left upper lobe pulmonary artery was pressed upon by the mass and there appeared to be some irregularity of the l. upper posterior apical pulmonary artery, suggesting the possibility of attachment to the vessel wall. In the latter films there appeared to be a compression upon the l. lateral inferior aspect of the aortic arch by the mass.

Bronchoscopy paralysis of l. vocal cord questionable slight deviation of vocal to right.

On the 13th hospital day an operation was performed.

CLINICAL DIAGNOSIS

Carcinoma of the lung.

Dr. Helen S. Pittman's* Diagnosis

Metastatic carcinoma of unknown origin to mediastinal lymph nodes.

ANATOMICAL DIAGNOSIS

Arteriosclerotic aneurysm of concavity of aortic arch.

*Associate Physician, Massachusetts General Hospital. Abstracted from the *New England J. Med.*, 253:931-934, 1955, with standing permission of the Editor.

## Exercise in the Disposition of Calories

Observations indicated that young men consuming high-fat diets were able to double their caloric supply without increasing the level of their serum lipids, so long as the excess energy was dissipated as exercise. The data suggested a downward trend of the serum cholesterol and lipoprotein levels during this period of high energy turnover. These findings support the concept that serum lipid levels are related to the caloric balance of the body.

Although the first days of physical training produced discomforts and fatigue, the men soon experienced a sense of well-being and accomplishment that they considered adequate compensation. During the period of low exercise and weight gain that followed, they continued to take excessive amounts of food without complaint and even with some relish, but as they grew fat they became sluggish and less efficient in their daily activities. Nevertheless, they were complacent while obesity progressed.

The first reaction may mean that physical condition is self-rewarding and sufficient motivation in itself aside from any desirable effects that it may have in preventing atherogenesis. The second reaction indicates that change of dietary habits, even when of short duration, are associated with great inertia. This tardiness of adjustment of food intake to metabolic requirements may be based on obscure physiological phenomena that are supplemental to the contribution made in real life by social customs, culinary artistry and changing values of pleasurable activities that occur with age.

Doubling the caloric supply of young men did not increase the serum lipoproteins and cholesterol levels when the surplus energy was expended as heat and muscular energy. Accretion of this excess energy as adipose tissue caused the serum lipid levels to increase in two of the three subjects.

It is proposed that positive caloric balance over a long period elevates the serum lipid levels and contributes to atherogenesis.

Mann, G. V., et al., *New England J. Med.*, 9:349-355, 1955.

### Acute Streptococcal Pharyngitis and Tonsillitis

The diagnostic features include abrupt onset with fever and sore throat, redness and edema of the pharynx, tonsils and soft palate, with a discrete-to-confluent yellow or white exudate, large tender cervical lymph nodes, and leucocytosis with a left shift.

Differential *infectious mononucleosis*—Onset more insidious, patients not as acutely ill, lymph node enlargement generalized, cervical not so tender, splenomegaly, usually lymphocytosis. *Diphtheria* onset is rarely sudden, sore throat not severe. Culture will reveal diagnosis. *Pharyngitis and tonsillitis of viral origin*—Onset insidious, patients are not acutely ill, sore throat moderate, not so firey red. *Vincent's angina* is usually unilateral, fever and constitutional symptoms unusual.

Hankey, D. D., *J. M. A. Georgia*, 9:450-460, 1955.

### Use of Nisentil Hydrochloride in Urology

A dose of 30 mg. Nisentil intravenously almost always produces immediate euphoria. Of the initial 25 patients, 7 complained of nausea (5 min.) Once this feeling had passed off, they were relaxed, calm and cooperative. Nausea and vomiting were minimized by 50 mg. Dramamine intramuscularly 20 to 30 minutes before the Nisentil. Since this has been established, only 1% have complained of nausea, and none have vomited. Residual discomfort, after action of Nisentil had worn off, was controlled by ½ gr. of codeine.

To date, Nisentil has been used, in doses of 30 mg. intravenously in more than 600 office procedures. There was only one reaction "urticarial" relieved by 2 cc. Benadryl, intravenously. The patients were 16 to 101 years of age with an average of 38 years.

Whether the patient was a 16-year-old girl or 101-year-old man, 30 mg. Nisentil intravenously given 20 to 30 minutes after 50 mg. Dramamine intramuscularly gave good analgesia. A cooperative patient lost his apprehension of having a cystoscopic or other urologic procedure. The effects would last the length of the procedure and the patient could get off the table, although a 30 minute rest in the supine position is advisable. There seems to be no contraindication, except possibly a definite urticaria.

We have used Nisentil HCl in more than 1,000 patients, and our results are the same.

Ashmore, A. J., et al., *Texas State J. Med.*, 7:463-465, 1955.



## "Half-minute" Thermometers

On a cold day it may take fiv minutes to record the body tem pera ture because the thermomet er i cold before insertion and chill s th tissues it contacts.

The difficulty can be easily ci cumvented by a simple mane uve which should be more w del known. The bulb is placed unde · on side of the tongue for ¼ of a mi ute this raises the temperature of th bulb to within a few degrees of th body temperature. The bulb is the slipped round to the opposite side o the tongue without being remove from the mouth and ½ minute later the thermometer is read. Total tim taken is ¾ of a minute, and the re sult is the same as leaving it on one side only for 5 minutes.

Freedman, B. J., *Brit. M.J.*, 4932:204, 1955.

## Trichomonas Vaginalis Infection in the Male

*T. vaginalis* infection is a majo disease problem. As in other proto zoal infections of man and animals it is probably also a general disease.

*T. vaginalis* infection of the male is becoming increasingly recognized. Infection is usually by sexual con tact, but contagion from fomites has been noted. Clinical and laboratory findings in both acute and chronic infection are described and refer ences made to latent infection and the carrier state. The possible exist ence of a transient trichomonemia is considered. Treatment of the acute stage is by urethral instillation of bactericidal drugs; chronic infec tion requires both general and local treatment.

Coutts, W. E., et al., *Brit. M. J.*, 4944:885-889, 1955.

# when neuritis strikes

## how long need it last?

Instead of enduring long weeks of pain and disability, your patients with inflammatory radiculitis (of non-traumatic or non-mechanical origin) can usually be quickly relieved with Protamide. When used promptly—within a few days after onset of pain—complete recovery can be expected in just a few days.

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*promptly*

*... one ampul daily, intramuscularly*

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A portfolio of all published studies will be sent on request

## Pulmonary Embolism

The one condition essential for pulmonary embolism is that a clot should form in any portion of the cardiovascular system peripheral to the pulmonary artery, and parts of this become detached and are carried by the blood stream into the pulmonary tree. The vast majority of emboli come from the deep veins of the legs, some from the pelvic veins, a few from the right side of the heart, a few from the venous channels in the upper extremities.

It occurs principally in patients strictly confined to bed, is rare in patients under 30 years of age, is as common in medical as in surgical cases, with a notably high incidence among those with heart disease, though in 90% of these the origin of the clot is in the peripheral veins.

A few cases occur in apparently healthy, ambulatory individuals.

Four results of sudden obstruction of the blood flow in the pulmonary arterial system are:

1. Pulmonary infarction due to the obstruction.
2. Acute cor pulmonale because of a sharp rise in the right ventricular pressure.
3. Peripheral vascular collapse.
4. Certain cardiac disorders.

However, pulmonary infarction, cor pulmonale or cardiac disorders may occur without any dramatic incident.

Sudden chest pain and fever are the commonest presenting features of pulmonary embolus and may be found without any other symptoms or signs. The diagnosis may be obvious or very difficult.

In the physical examination of the case of suspected embolism, on no account should the patient be asked to breathe deeply to facilitate auscultation of the chest. Death has occurred under such circumstances following the sucking of a large clot into the chest. The administration of adequate laxatives is also important to avoid straining at stool.

Hunter, R. B., *Brit. M. J.*, 4927:1424, 1955.

## Hiatus Hernia, Gallstones and Diverticulosis Coli

Routine clinical investigation of 170 adult patients with hiatus hernia revealed that 24 (14%) also had gallstones *and* diverticulosis coli (Saint's triad). This, and information from the literature suggest that, when a hiatus hernia patient is found to have either gallstones or diverticulosis, there is an excellent chance that the third disease is also present.

When there was a noncritical assumption that gallbladder disease was responsible for the patients' illness, symptomatic results of cholecystectomy were poor.

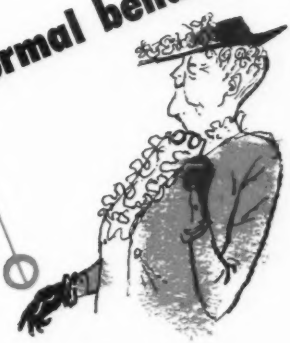
Palmer, E. D., *Am. J. Digest. Dis.*, 22:314-315, 1955.

## How to Provoke Amebae Appearance

The patient buys 500 gm. skimmed milk powder and prepares 2 days before the laboratory examination by taking 200 gm. in 2 liters of water per day; the patient can enjoy it with milk, coffee, cacao (always boiled), with or without sugar as preferred. This drink causes a diarrhea generally on the second day of its use and if the amebae in any form are present, they will appear in the diarrheic stool presented freshly on those days to the laboratory.

Weiser, J., *Am. J. Digest, Dis.*, 10:296, 1955.

FROM CONFUSION to a normal behavior pattern



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1. Levy, S., *J.A.M.A.*, 153:1260, 1593.
2. Thompson, L., Procter, R., *North Carol M. J.*, 15:596, 1954.

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## Rheumatic and Non-Rheumatic Leg-Pains

Children with subacute rheumatic fever commonly give a history of a sore throat or upper respiratory infection a week or more before the onset of pain in joints, usually both upper and lower extremities, progressing from one joint to another. These children point directly to a knee, ankle, or wrist. Involved joints show local heat, slight swelling, and tenderness on deep pressure; pain usually persists the entire day, is worse on motion, and often causes a limp. Relief of pain is usual on getting into bed, rarely is there a cry out at night because of pain. On awakening, joints and muscles are stiff; some time elapses before they can move around comfortably. Evidence of low-grade infection—low fever, pallor, nosebleeds, lack of appetite, failure to gain weight. Auscultation from day to day may reveal a systolic or diastolic murmur; repeated ECG may trace a developing myocarditis; x-ray studies, an increase in the size of the heart.

In our anxiety to prevent cardiac involvement, we should be careful not to label healthy children with this diagnosis.

Shapiro, M. J. *Modern Concepts of Cardiovascular Disease*, 10:295-297, 1955.

## Auscultation of the Abdomen

Recently, a Dublin surgeon summarized his many years of experience in listening to the gurglings and growls of abdominal organs.

The routine practice of abdominal auscultations will decrease the risk of serious diagnostic error in difficult cases.

In *perforation* with considerable spill of intestinal contents and free air into the peritoneal cavity, one may hear a fairly sharp click or slapping sound in the epigastrium, synchronous with respiration, occurring at the same point in each respiratory cycle.

Early in *acute appendicitis*, the abdominal sounds are normal. Local peritoneal irritation leads to increased activity of the gut in the right lower quadrant. As peritonitis advances, the sounds of bowl hypermotility spread, to be followed by complete cessation of intesinal movements — "the silent abdomen" — in general peritonitis.

*Paralytic ileus*, when fully developed, has its characteristic "melody." Upon listening for several minutes, one hears a high-pitched, passive sound as a few gas bubbles rise to the surface of a tense loop of intestine shifted by respiratory or external movement. In addition, a small, high-pitched tinkle may be audible. These two sounds signify an advanced ileus.

In *intestinal obstruction*, bursts of accentuated bowel sounds coincide with the painful, colicky spasms being experienced by the patient. This helps to distinguish various types of abdominal pain.

In young children and also in cases of generalized peritonitis, heart sounds are sometimes clearly heard over the iliac fossae.

Walsh, A., *J. Irish M. A.*, 36:48, 1955.

## Status Asthmaticus

By use of the adrenocortical steroids status asthmaticus attacks can now be ameliorated quickly. Oxygen or helium-oxygen mixtures have no advantage over room air for the sick asthmatic.

*Disease Panorama* (Schering Corporation), 1955.

Of all the hundreds of papers that have been published on the subject of Medical Ultrasonics, one of the most enlightening to the G.P. is the report by another small town General Practitioner, published in the August issue of Medical Times magazine. This paper covers the use of ultrasonic therapy in the treatment of patients who had **previously failed** to respond to other methods. The report includes cases of:

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We will mail you a reprint of this article on request. We also have on hand a large collection of reprints which cover a host of other diseases. Included is the bound collection of all 17 papers presented at the 4th Annual Conference of the American Institute of Ultrasonics in Medicine which was held August 27th, 1955 in Detroit, Michigan. If you have patients who are not responding to other treatment and would like to have the free use of an ultrasonic machine for one month, we will be happy to arrange for one of our dealers to put a Birtcher Megason in your office . . . no charge or obligation, of course.

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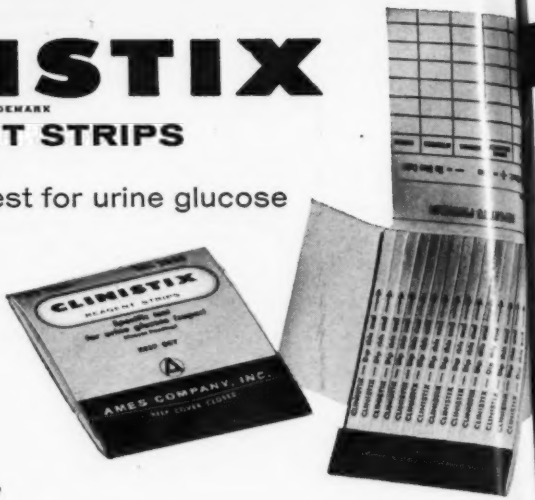


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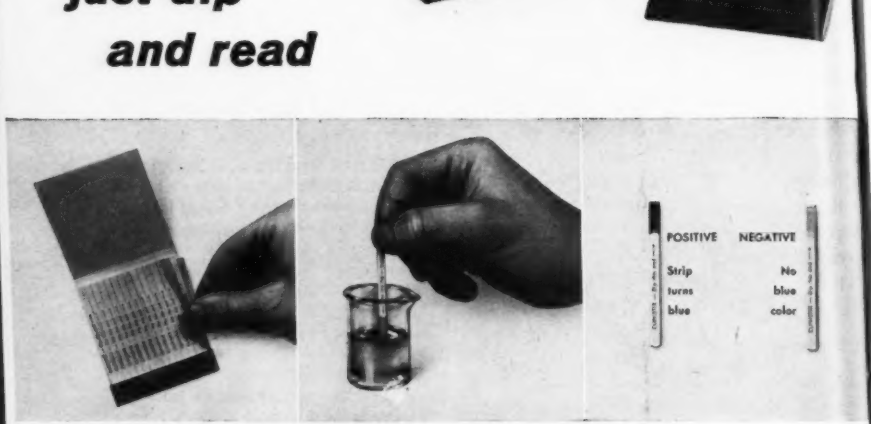


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**Rectal Desitin Ointment** *(Desitin)*

A tacky consistency permits this ointment to adhere firmly to the mucous membrane for long-lasting relief. A wetting agent allows even coverage of engorged blood vessels to assure utilization of medication. Contains no local anesthetics, narcotics or "caine" derivatives, so does not mask serious anorectal disease. It contains Norwegian Cod Liver Oil, zinc oxide, lanolin, talcum, sodium lauryl sulfate, and petrolatum q.s. *Indications:* non-surgical hemorrhoids, anorectal irritation, pruritus, uncomplicated fissures, proctitis, inflammatory cryptitis, papillitis and perianal dermatitis. *Supplied:* 1½ oz. tube with safe, flexible applicator.

**Neobon Liquid** *(Roerig)*

A tonic which promotes hematinic action and improved protein and carbohydrate utilization by supplementing gonadal and thyroid hormone production, inducing a mild, antidepressant effect. Each 5 cc. teaspoonful contains 1 mcg. ethinyl estradiol, 1 mg. methyltestosterone, 25 mg. liver fraction 1 N. F., 2.5 mcg. vitamin $B_{12}$, O.17 mg. folic acid, 50 mg. vitamin C, 30 mg. ferrous gluconate, 0.1 mg. 1-thyroxine, 0.5 mg. d-amphetamine sulfate and 10 per cent alcohol. *Indications:* nutritional, physiological and mental depression in persons of the middle and older age groups. *Dosage:* one teaspoonful twice daily before meals, or as required. *Supplied:* bottles of 16 fluid ounces.

**B-Telve** *(Paul Maney)*

Appetite-stimulating and growth-promoting tablets designed particularly for older children and adults. Each tablet contains 25 mcg. of Vitamin $B_{12}$ and 10 mg. of Vitamin $B_1$. *Indications:* poor appetite, undernourishment, chronic illnesses, etc. *Dosage:* one tablet daily or as directed by the physician. *Supplied:* bottles of 100 and 1000 tablets.

**Flexin** *(McNeil)*

Generically zoxazolamine, a newly synthesized compound unrelated to any available agent. Eliminates muscle spasm without interfering with normal muscle power or activity. Its action is primarily central, in the spinal cord and subcortical areas of the brain. It is slowly absorbed, effective to six hours, rapidly metabolized and excreted. *Indications:* low back pain, fibrositis, spondylitis and rheumatoid arthritis; and spinal spasticity states, cerebral palsy, multiple sclerosis, cerebral vascular accidents and Parkinson's disease. *Supplied:* bottles of 50 yellow scored tablets of 250 mg. each.

**Hydrocortisone Acetate Aqueous** *(Philadelphia Ampoule)*

Suspension, 25 mg./cc. in normal saline. *Indications:* acute or active localized inflammatory sites. *Administration:* intra-articular injection. *Caution:* read insert before administering. *Supplied:* 5 cc. multiple dose vial.

**Calcidrine** *(Abbott)*

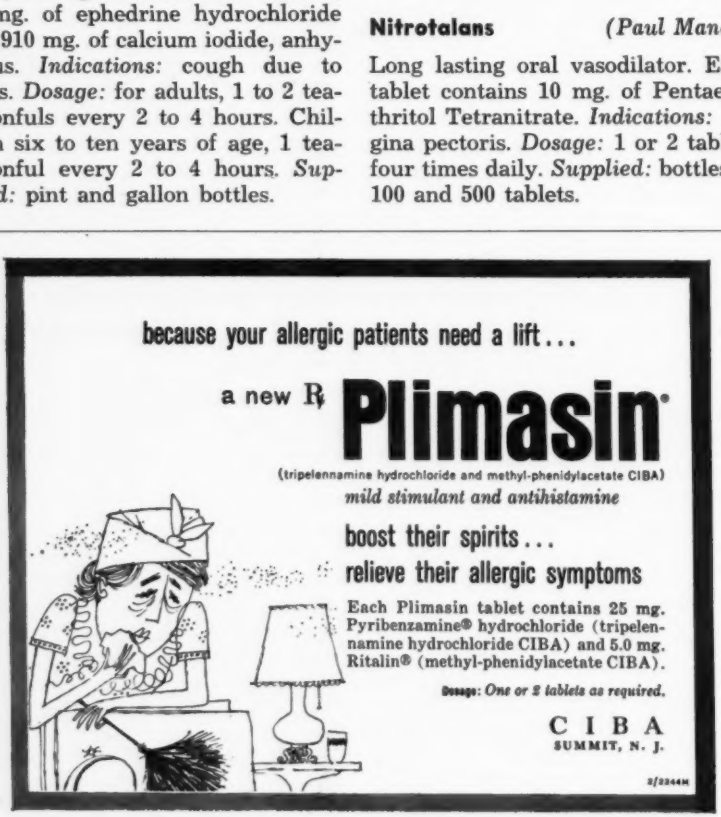
Mucous liquifying, antispasmodic and sedative action with apricot flavor and color. Each cc. contains 10 mg. of dihydrocodeinone bitartrate, 25 mg. of Nembutal sodium, 25 mg. of ephedrine hydrochloride and 910 mg. of calcium iodide, anhydrous. *Indications:* cough due to colds. *Dosage:* for adults, 1 to 2 teaspoonfuls every 2 to 4 hours. Children six to ten years of age, 1 teaspoonful every 2 to 4 hours. *Supplied:* pint and gallon bottles.

**Rutaminal-RQ** *(Schenley)*

Cardiovascular adjuvant tablet. A change in the basic "Rutaminal" formula whereby reserpine replaced phenobarbital and quercetin supplants rutin. Each tablet contains 100 mg. of aminophylline, 15 mg. of quercetin, 25 mg. of ascorbic acid and 50 mcg. of reserpine. *Indications:* coronary artery disease, arteriosclerosis, angina pectoris, hypertensive vascular disease, etc. *Dosage:* 4 tablets daily, one after each meal and one at bedtime. *Supplied:* bottles of 100 and 1000 tablets.

**Nitrotalans** *(Paul Maney)*

Long lasting oral vasodilator. Each tablet contains 10 mg. of Pentaerythritol Tetranitrate. *Indications:* angina pectoris. *Dosage:* 1 or 2 tablets four times daily. *Supplied:* bottles of 100 and 500 tablets.

# THERAPEUTIC TRENDS

## Blood Levels From Orally Administered Penicillins G and V

In a controlled study of levels in blood, using 200,000 units of penicillin G and V, V produced higher and more prolonged levels than G; this was particularly striking when the comparisons were made with the doses that were taken after breakfast.

Jones, Jr., W. F., et al, *New England J. Med*, 18: 754-761, 1955.

## Drug Trial and Error Necessary in Epilepsy

Finding the most suitable anticonvulsant and right dose in treating epilepsy requires from 3 to 6 months. The trial-and-error method is inescapable.

Mebaral is recommended either alone or combined with other safe anticonvulsants in the treatment of all types of convulsive disorders, before using any of the newer dangerous drugs. It is a particularly valuable adjunct in petit mal seizures since it enhances the response of the companion drug and reduces the chance of worsening a grand mal seizure. Mebaral permits use of a smaller dose of the second drug, thereby decreasing the chance of toxic effects.

Drake, F. R., *American J. Med.*, 230:98, 1955.

## Methenamine Therapy

The author emphasizes that there has been a trend in some medical circles to overlook older but more reliable drugs in favor of newer, untried medicaments that have not stood the test of time. A case in point is that of Methenamine*, which he has found most useful in the treatment of cases of cystitis which have not responded to the use of multiple types of antibiotics. He has found that this preparation is helpful in older patients with chronic urinary infections associated with urinary retention. It clears infected urine and establishes rapid relief from burning urination. In chronic cases, Methenamine can be prescribed over lengthy periods of time, without inducing drug-fastness.

*Urolitia, Borcherdt Malt Extract Company, Chicago, Ill.
Marshall, W., *Mississippi Doctor*, 33:260-261,1956.

## Nausea and Vomiting of Uremia

Chlorpromazine, a new antiemetic agent, was successfully used in the control of nausea and vomiting in 15 severely uremic patients. No serious adverse effects were noted from short-term administration.

Schreiner, G. E., *Med. Ann. District of Columbia*, 24:116-158, 1955.

## Simple Apparatus for Resuscitation of Asphyctic Newborns

Gentleness is essential in the treatment of asphyxia of the newborn. Available oxygen apparatus for this purpose is expensive. The author worked out a small apparatus which has proved its value. The oxygen is taken from one of the usual tanks with a manometer, reducing valve and moistener, and the desired number of liters per minute is set by means of a flowmeter.

The oxygen current flows through a rubber tube into a breathing bag of 2 liters capacity connected with a mask; a safeguard against excessive pressure is placed into this pathway in the form of a glass cylinder containing water into which a T tube is immersed to a variable depth regulating the maximal pressure, which should not be exceeded. The asphyctic newborn is placed in a Trendelenburg position of 15 degrees after cleansing of the upper respiratory tract with the tracheal catheter. The mandible is held slightly forward and upward and the small mask is placed cautiously but tightly over the mouth and nose. By rhythmic pressure on the breathing bag with a frequency of 20 to 30 per minute, artificial respiration is effected.

Niggli, G., *Gynaecologia*, 137:260, 1954.

## Cites Benefits in Emphysema of Isuprel in Aerosol Form

Isuprel given 3 to 4 i.d. is one of the most effective aerosolized bronchodilators. More intensive use of Isuprel, with limited amounts of oxygen is in order when respiratory acidosis occurs.

Miller, R. D., *Arch. Int. Med.*, 96:360, 1955.

## Recent Developments in Diarrhea of the Newborn

In many epidemics of diarrhea of the newborn, the etiology is still not known, although *E. coli* serogroups are being reported with increasing frequency. Since many strains of *E. coli are* susceptible to neomycin, this drug has been used to treat cases of *E. coli* diarrhea throughout the hospital stay, and as prophylactic medication in well infants and nursery personnel to check the further spread of an epidemic. It is now recommended that infants admitted to hospitals be carefully screened, isolated, and if necessary treated with neomycin.

Greene, D. C., et al., *New York State J. Med.*, 55: 2764-2768, 1955.

## Lente Insulin in the Treatment of Diabetes

Lente insulin has a duration of action of 24 hours. Its action closely resembles that of isophane (NPH) insulin, and the two types may, in general, be used interchangeably. Crystalline insulin may be given in a single injection with lente insulin just as with NPH insulin, with preservation of most of the rapid action of the unmodified type. This procedure is practicable and effective clinically.

A few patients, particularly children, complain of discomfort at the site of injection greater than that with other types of insulin, presumably due to a difference in the type of preservative. Allergy to lente insulin does occur, but to date it is less frequent than that of other varieties.

Slayton, R. E., et al., *New England J. Med.*, 17: 722-725, 1955.

# RIASOL

## *LOCAL* TREATMENT IN PSORIASIS

recent survey of medical literature es that dermatologists definitely prefer to internal therapy for psoriasis.

or example, Solomon, Netherton, Nelson Zeiter* in 1955 said: "Psoriasis is a fre- tly recurrent common skin disease that esistant to treatment. Of the various ments devised for it, the topical ones are erior to the internal ones."

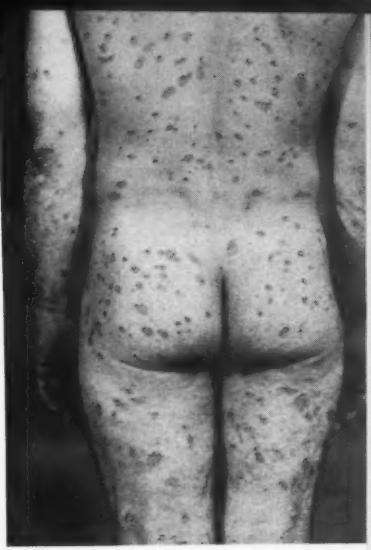
IASOL is one of the most widely used of ocal therapies for psoriasis. In most cases lears the skin of the scaly patches of riasis, or greatly reduces them, in a period eeks. If applied for several weeks after visible lesions have disappeared, RIASOL also prevent recurrence.

IASOL contains 0.45% mercury chem- ly combined with soaps, 0.5% phenol 0.75% cresol in a washable, non-staining, rless vehicle.

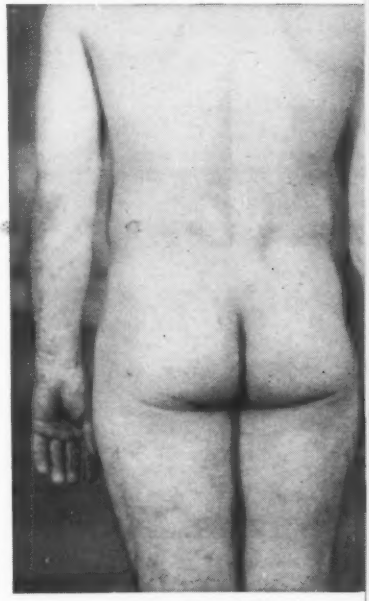
pply daily after a mild soap bath and rough drying. A thin, invisible, eco- nical film suffices. No bandages required. er one week, adjust to patient's progress.

IASOL is supplied in 4 and 8 fld. oz. tles at pharmacies or direct.

omon, W. M., Netherton, E. W., Nelson, P. A. & Zeiter, W. J., *A.M.A.* 157:1349,1955 (abstract).



Before Use of Riasol



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# RIASOL for PSORIASIS

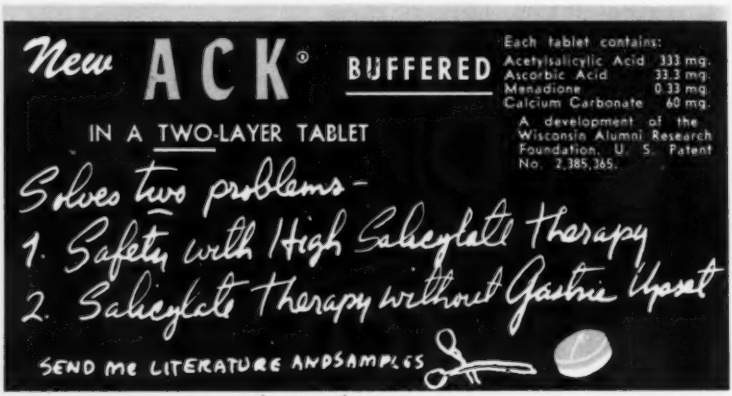
**Sudden Giddiness**

The management of an acute attack of giddiness is the same whatever its cause. Meniere's disease is by far the commonest cause.

The patient should be allowed to lie in a comfortable position of his own choosing as soon as possible. Patient and family must be reassured. The episode is alarming, but it will subside in a few hours and is never fatal or paralysing. No drug has a specific effect on vertigo, but an IM injection of sodium phenobarbitone, 3 gr. stat, plus oral phenobarbitone ½ gr. to 3 i.d. should be continued for some weeks afterwards and when the patient feels that attacks are "just around the corner." In Meniere's disease seasickness remedies such as hyoscine and antihistamines — promethazine and dimenhydrinate — may be helpful, but are in no way specific. Fluids restricted for a week or two to 2 pints in 24 h. and salt omitted from cooking and at table. This "antitentional" regimen the patient should adopt when he expects an attack.

Most patients who have been reassured manage reasonably well by restricting their activities, using phenobarbitone, learning to recognize premonitory symptoms, and going to bed. When periods of remission do not occur and attacks cannot be modified by these measures, the question of destruction of one labyrinth by alcohol injection, diathermy, or removal of the external semicircular canal will have to be considered.

Spillane, J. D., *Brit. M. J.*, 4939:612-614, 1955.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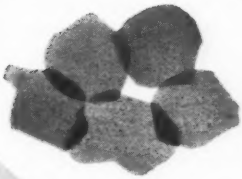

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## Treatment of Traumatic Scalp Wounds

There is no need for trimming the wound edges, since the edges come together correctly in spite of their irregularity. Nor has it been necessary to tie blood vessels in any of the "superficial" or "deep" cases.

Use a 1:1000 solution or hexylresorcinol (soap and water or normal saline solution may be used) to wash out foreign particles. *The scalp is not shaved,* nor is any attempt made to remove the hair at the edges of the wound. Any hair falling into the wound is gently picked out with tissue forceps and placed aside; none of the hair is shaved or clipped. X-rays of the skull are taken in all traumatic wounds of the scalp. The wound is then dusted with sterile oxytetracycline powder. Whether the wound be superficial or deep, the skin edges are brought together with Michel clips placed ⅜ in. apart. With firm placement of the clips, hemostasis occurs immediately, and the scalp edges come together completely and without inversion. Local anesthesia is not used; nor is it needed.

In the event of avulsion of the scalp, following the cleansing, x-ray examination and dusting, the muscles and fascia are closed with 00 chromic catgut, more powder is dusted into the wound, and clips unite the skin edges.

*Dressings are not applied.* The hair is pulled over the area, thus covering clips and laceration. On a bald scalp 3 x 3 gauze squares are placed over the wound, and a stockinette cap.

Penicillin, 500,000 units is given those patients with a negative history of penicillin allergy, a 2nd inspection in 24 hours if much dir and trauma. A routine practice s th use of either tetanus antitoxin te anus antitoxin and gas bacillus vac cine, or tetanus toxoid.

The patient returns in 24 h urs if a firm crust is present the clip are removed in most instances. Th patient is careful when combi g o brushing the hair. Clips not remove in first 24 hours are removed afte 48 hours. Separation of edges ha not occurred in any of the cas es.

Patients keep the scalp dry 5 to 7 days. A final examination of the wound is done in 5 days, and the patient discharged.

The arrangement of the blood supply enables the scalp to survive even though a considerable portion is detached from the cranium. It is unnecessary to do extensive debridement of scalp tissue when it is injured.

Frohman, I. P., *GP*, July, 1955.

## Treatment of 200 Disturbed Psychotics With Reserpine

Reserpine is of definite value in the treatment of chronically disturbed psychotic patients; 22% of a group of 200 such patients have improved sufficiently to be judged well enough to leave the hospital; 86% showed some degree of improvement, and 71% did better with reserpine therapy than with electroshock. Although certain toxic effects of reserpine (including Parkinsonism and convulsions) were observed in the treated patients, all of them disappeared when the dosage was reduced.

In 78%, improvement has been maintained after medication was discontinued.

Barsa, J. A., et al., *J.A.M.A.*, 158:110-113, 1955.

## Experiences with New Delayed Action Insulins in Diabetes of Childhood

The standard mixture of *insulin lente* is suitable particularly for control of new cases of diabetes in childhood.

The results with insulin lente were less convincing in older cases in which other insulins had been used before, and individual mixtures of the semilente and ultralente components were frequently required.

Correction of the C reaction by addition of the semilente component seems easier and more successful than that of the A reaction by addition of the ultralente component.

Cases with a forenoon hyperglycemia are still more difficult to control as the semilente component has no marked effect in the first 4 hours after injection, and on the other hand, an increase of the dosage will still further reduce the low p.m. blood sugar level.

Therefore an admixture of old insulin would be necessary for the a.m. hours; shifts in the carbohydrate intake may be used for prevention of the a.m. hyperglycemia but the possibilities of such shifts are limited in school children, and also by the eating habits.

In unstable cases an attempt to control by the insulin zinc suspensions is advisable although requiring much patience; vegetative sedatives are indicated in such cases.

The authors do not believe in the advantages of the so-called free diet and insist on adherence to a high-carbohydrate low-fat diet.

The local tolerance to insulin lente is excellent and hypersensitivity reactions to other delayed action insulins form an indication for a change to this preparation.

Disagreeable protracted hypoglycemia of the central nervous system, often the cause of school difficulties of diabetic children, seems less frequent with insulin lente than with other insulins. The possibility of individual combinations of the two components of insulin lente is an advantage, but makes treatment more complicated. Final judgment of the value of the new insulin type will have to wait until an observation period of several years has passed.

Swoboda, W., et al., *Schweiz. Woch.* 85:231, 1955.

## Toxic Effects of Phenylbutazone

Since its first use four years ago, phenylbutazone (Butazolidin) has been employed extensively in hospitals and in general practice, and many reports on its use have appeared in the medical press. There is general agreement that the drug has a marked analgesic action in rheumatoid arthritis in one case in three, but it is doubtful whether it has any anti-inflammatory properties.

A fatal case is reported in which six complications developed during the administration of the drug — ulceration of the lips and mouth, rash, hematemesis, perforation of a gastric ulcer, jaundice and a polyneuritis. Their causal relationship to the use of the drug is discussed. The possible factors in the production of side-effects are mentioned.

It is felt that phenylbutazone is a dangerous drug and should not be employed in the treatment of rheumatoid arthritis. Aspirin given in maximum tolerated doses is as effective and much less toxic.

Fraser, T. N., *Brit. M. J.*, 4925:1318-1320, 1955.

## Preoperative Care and Premedication

Every patient should be visited preoperatively by the anesthesiologist. The patient welcomes the opportunity to disclose anything pertinent regarding previous anesthesia or his health, asks questions regarding the proposed anesthesia. If a spinal injection is to be used, the patient should be told so without subterfuge.

Calm assurance that the best agents and methods will be used skillfully will go a long way toward establishing the patient's confidence. Say that you will use the agents and methods that provide most comfort within the limits of safety and conditions for the surgeon to work to best advantage of patient.

He is told that he may receive a capsule and injection in his room, and that he will feel sleepy or groggy as he arrives in the operating theater. Allay any fears.

The patient should be greeted by name and transferred gently to the table. Quiet words of assurance rather than restraints are used during induction. Question regarding palpitation, shortness of breath, ankle edema, ability to exercise, duration and severity of the present illness, any previous anesthesia, drug sensitivity.

If the patient says he is a "bleeder" recheck the bleeding, clotting, and prothrombin time. Any pertinent data (clinical or laboratory) from the chart should be summed up and recorded on the anesthesia record.

An apprehensive patient should be given one of the short-acting barbiturates 1½ to 2 hours before operation; to the elderly, morphine or Demerol, according to age and BMR. The maximum sedative effect of morphine is in 90 minutes.

Atropine inhibits secretions, counteracts the respiratory depression of morphine to some extent, and reduces laryngospasm, especially that resulting from Pentothal. Scopolamine has greater drying action depresses rather than stimulates the cortical centers, and produces a degree of amnesia and sedation.

Atropine is preferable in the elderly patient. Ration of 25:1 between morphine and a belladonna drug is optimum.

Ausherman, H. M., *North Carolina M. J.* 10:492-496, 1955.

## For Herpes Zoster: Application of Hydrocortisone

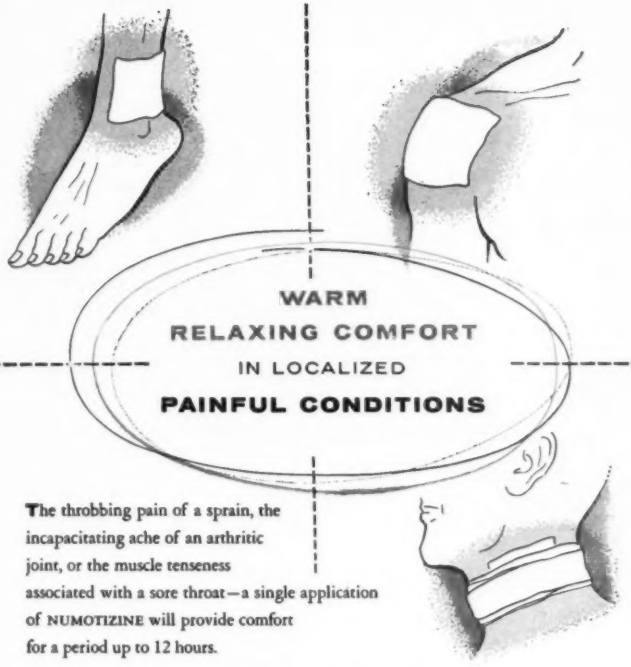
An opportunity to observe 3 cases of herpes zoster within a period of a month, permitted a study of the response to this disease to the topical application of 1% hydrocortisone.

Without exception, response to treatment was prompt and gratifying. Duration of this self-limited disease was symptomatically reduced from weeks to days; most striking was the amelioration of both pain and skin lesions. Sleepless nights disappeared. Within 24 to 96 hours, patients could resume their occupations. In no instance did a relapse occur. Application of ointment twice daily was made until pain and inflammation had regressed completely.

No systemic effects or complications were noted.

Topical application of 1% hydrocortisone affords a simple, effective treatment for herpes zoster.

Marshall, F. A., *J. M. Soc. New Jersey*, 9:474-475, 1955.



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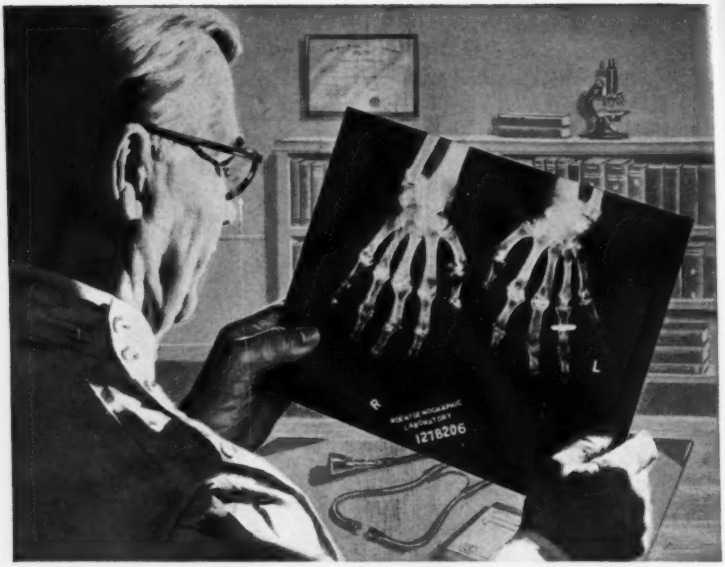


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Treatment of rheumatoid arthritis demands a "highly individualized program," Spies[1] writes. The additive action of salicylates permits use of smaller amounts of hormones, thus lessening or eliminating their well-known side effects. "A proper mixture of salicylates and corticosteroids produces an effective antirheumatic agent in many cases."[1]

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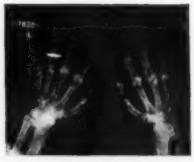

**References:**
1. J. A. M. A. 159:645 (Oct. 15) 1955. 2. J.A.M.A. 158:386 (June 4) 1955.

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# BOOK REVIEWS

## A Handbook of Hospital Psychiatry

*A Practical Guide to Therapy, by Louis Linn, M.D., Assistant Attending Psychiatrist, Mount Sinai Hospital, New York City. International Universities Press, Inc., 227 West 13th St., New York 11, N. Y. 1955. $10.00*

It is said of this book that it is a new approach to the teaching and practice of clinical psychiatry, that it sets forth the daily needs of the professional staff of the mental hospital and discusses the working out of solutions of their problems. The book is based on broad professional experience in state, army and general hospitals as well as in psychoanalysis.

Each chapter is followed by a carefully chosen list of references, and a number of appendices make the book of greater practical usefulness.

## The Relief of Symptoms

*by Walter Modell, M.D., F.A.C.P., Associate Professor of Clinical Pharmacology, Cornell University Medical College. W. B. Saunders Company, Philadelphia. London. 1955. $8.00.*

Many "very modern" doctors speak disparagingly about "symptomatic" treatment; but when these very doctors have symptoms themselves, they loudly demand that these symptoms be relieved.

The authors say "this book is offered as a practical guide to the problems of providing the patient with relief from his distress." Among the distresses for which means of relief are given are pain, anxiety, insomnia, gas, constipation, diarrhea, loss of appetite, obesity, palpitations, edema, dyspnea, cough, weakness and fatigue, nausea and vomiting, vertigo, itching, hiccups, unconsciousness, convulsions, muscle spasm, menstrual disorders, dysuria and jaundice.

There is a chapter on "Cortisone and the masking of symptoms."

Every practitioner of medicine and surgery should have a copy and put its teaching into daily use.

## Cardiac Diagnosis: A Physiologic Approach

*by Robert F. Rushmer, M.D., Associate Professor of Psychology and Biophysics, University of Washington Medical School. Illustrated. W. B. Saunders Company, Philadelphia. London. 1955. $11.50.*

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REFERENCES

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2. Gitman, L., and Koplowitz, A.: N. Y. St. J. Med. 50:2823, 1950.
3. Karnaky, K. J.: South. M. J. 45:1166, 1952.
4. Peña, E. F.: Med. Times 82:921, 1954; Am. J. Surg. 87:95, 1954.
5. Ross, J. W.: J. Nat. M. A. 43:20, 1951; 45:223, 1953.


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